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(71) Applicant *(for all designated States except US)*: **LIGAND PHARMACEUTICALS INCORPORATED** [US/US]; 10275 Science Center Drive, San Diego, CA 92121 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **ZHI, Lin** [CN/CA]; 7794 Roan Road, San Diego, CA 92121 (US). **TEGLEY, Christopher** [US/US]; 13328 Caminito Ciera #10, San Diego, CA 92129 (US). **PIO, Barbara** [US/US]; 3319 Bevis Street, San Diego, CA 92111 (US). **ARJAN VAN OEVEREN, Cornelis** [NL/CA]; 7675 Palmilla Drive #6315, San Diego, CA 92122 (US). **MOTAMEDI, Mehrnouch** [US/US]; 7560 Charmant Drive #1532, San Diego, CA 92122 (US). **MARTINBOROUGH, Esther** [US/US]; 5220 Fiore Terrace #303, San Diego, CA 92122 (US). **WEST, Sarah** [US/US]; 7932 Port Royale Drive, San Diego, CA 92126 (US). **HIGUCHI, Robert** [US/US]; 434 Marview Drive, Solana Beach, CA 92075 (US). **HAMANN, Lawrence** [US/US]; 190 Del Mar Shores Terrace #61, Solana Beach, CA 92075 (US). **FARMER, Luc** [US/US]; 19 Howe Lane, Foxborough, MA 02035 (US).

(74) Agents: **PAGLIERY, Richard** et al.; Brobeck, Phleger & Harrison, LLP, 12390 El Camino Real, San Diego, CA 92130 (US).

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(54) Title: BICYCLIC ANDROGEN AND PROGESTERONE RECEPTOR MODULATOR COMPOUNDS AND METHODS

(57) Abstract: The present invention is directed to compounds, pharmaceutical compositions, and methods for modulating processes mediated by AR and PR. More particularly, the invention relates to nonsteroidal compounds and compositions that are high affinity, high specificity agonists, partial agonists (i.e., partial activators and/or tissue-specific activators) and antagonists for AR and PR. Also provided are methods of making such compounds and pharmaceutical compositions, as well as critical intermediates used in their synthesis.

BICYCLIC ANDROGEN AND PROGESTERONE RECEPTOR MODULATOR COMPOUNDS AND METHODS

This application claims priority to U.S. Provisional Application No. 60/150,987, filed August 27, 1999, the entire disclosure of which is incorporated by reference herein.

Field of the Invention

This invention relates to nonsteroidal compounds that are modulators (i.e., agonists, partial agonists and antagonists) of androgen and progesterone receptors, and to methods for the making and use of such compounds.

Background of the Invention

Intracellular receptors (IRs) form a class of structurally-related genetic regulators scientists have named "ligand dependent transcription factors" (R. M. Evans, *Science*, 240:889, 1988). Steroid receptors are a recognized subset of the IRs, including androgen receptor (AR), progesterone receptor (PR), estrogen receptor (ER), glucocorticoid receptor (GR), and mineralocoticoid receptor (MR). Regulation of a gene by such factors requires both the IR itself and a corresponding ligand, which has the ability to selectively bind to the IR in a way that affects gene transcription.

The natural hormones for steroid receptors have been known for a long time, such as testosterone for AR and progesterone for PR. A synthetic compound that binds to an IR and mimics the effect of the native hormone is referred to as an "agonist", while a compound that inhibits the effect of the native hormone is called an "antagonist". The term "modulators" refers to a group of compounds that have a spectrum of activities from agonist, partial agonist to antagonist.

Androgen and progesterone receptor modulators are known to play an important role in health of both men and women. For example, AR antagonists, such as cyproterone acetate, flutamide and casodex, are useful in the treatment of prostatic hyperplasia and cancer of the prostate. AR agonists, such as fluoxymesterone, are used in the treatment of hypogonadism. PR agonists, such as medroxyprogesterone acetate, are used in birth control formulations in combination with the female hormone estrogen or a synthetic estrogen analogue. Further,

antagonists of PR are potentially useful for contraception and in the treatment of chronic disorders, such as certain hormone dependent cancers of the breast, ovary and uterus. Due to increased life expectancies, development of tissue selective, safer, orally active AR and PR modulators are desirable to improve quality of life.

A group of hydroquinoline derivatives was recently described as AR and PR modulators (e.g., U.S. Patent Nos. 5,688,808, 5,688,810, 5,693,646, 5,693,647, 5,696,127, 5,696,130). This group of AR and PR modulators was developed by using cell-based high-throughput assays, termed cotransfection assays. Amino- or hydroxy-trifluoromethylquinolones or coumarins have been described as fluorescent markers in biological systems. See, e.g., U.S. Pat. No. 4,505,852 and E. R. Bissel et al., "Synthesis and Chemistry of 7-Amino-4-(trifluoromethyl)coumarin and Its Amino Acid and Peptide Derivatives", *J. Org. Chem.*, 45:2283, 1980). Analogues of quinolone, oxindole, benzooxazinone derivatives have been described as cardiotonic agents. See, e.g., U.S. Patent Nos. 3,993,656; 4,415,572; 4,427,654; 4,710,507; 4,728,653; 4,933,336; 5,081,242.

Summary of the Invention

The present invention is directed to compounds, pharmaceutical compositions, and methods for modulating processes mediated by AR and PR. More particularly, the invention relates to nonsteroidal compounds and compositions that are high affinity, high specificity agonists, partial agonists (i.e., partial activators and/or tissue-specific activators) and antagonists for AR and PR. Also provided are methods of making such compounds and pharmaceutical compositions, as well as critical intermediates used in their synthesis.

For a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying descriptive matter, in which preferred embodiments of the invention are described.

Detailed Description of Preferred Embodiments

In accordance with the present invention and as used herein, the following structure definitions are provided for nomenclature purposes. Furthermore, in an effort to maintain consistency in the naming of compounds of similar structure but differing substituents, the compounds described herein are named according to the following general guidelines.

The term "alkyl" refers to an optionally substituted straight-chain or branched-chain hydrocarbon radical having from 1 to about 10 carbon atoms, preferably from 1 to about 6 carbon atoms, and most preferably from 1 to about 4 carbon atoms. Examples of alkyl radical include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, pentyl, hexyl, octyl and the like.

The term "alkenyl" refers to a straight-chain or branched-chain hydrocarbon radical having one or more carbon-carbon double-bonds and having from 2 to about 10 carbon atoms, preferably from 2 to about 6 carbon atoms, and most preferably from 2 to about 4 carbon atoms. Preferred alkeny groups include allyl. Examples of alkenyl radicals include ethenyl, propenyl, 1,4-butadienyl and the like.

The term "allyl" refers to the radical $H_2C{=}CH{-}CH_2^{\cdot}$.

The term "alkynyl" refers to a straight-chain or branched-chain hydrocarbon radical having one or more carbon-carbon triple-bonds and having from 2 to about 10 carbon atoms. Examples of alkynyl radicals include ethynyl, propynyl, butynyl and the like.

The term "aryl" refers to optionally substituted aromatic ring systems. The term aryl includes monocyclic aromatic rings, polycyclic aromatic ring systems, and polyaromatic ring systems. The polyaromatic and polycyclic ring systems may contain from two to four, more preferably two to three, and most preferably two, rings. Preferred aryl groups include 5-or 6-membered aromatic ring systems.

The term "heteroaryl" refers to optionally substituted aromatic ring systems having one or more heteroatoms such as, for example, oxygen, nitrogen and sulfur. The term heteroaryl may include five- or six-membered heterocyclic rings, polycyclic heteroaromatic ring systems, and polyheteroaromatic ring systems where the ring system has from two to four, more preferably two to three, and most preferably two, rings. The terms heterocyclic, polycyclic heteroaromatic, and polyheteroaromatic include ring systems containing optionally substituted heteroaromatic rings having more than one heteroatom as described above (e.g., a six membered ring with two nitrogens), including polyheterocyclic ring systems from two to four, more preferably two to three, and most preferably two, rings. The term heteroaryl includes ring systems such as, for example, pyridine, quinoline, furan, thiophene, pyrrole, imidazole and pyrazole.

The term "alkoxy" refers to an alkyl ether radical wherein the term alkyl is defined as above. Examples of alkoxy radicals include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, iso-butoxy, sec-butoxy, tert-butoxy and the like.

The term "aryloxy" refers to an aryl ether radical wherein the term aryl is defined as above. Examples of aryloxy radicals include phenoxy, benzyloxy and the like.

The term "cycloalkyl" refers to a saturated or partially saturated monocyclic, bicyclic or tricyclic alkyl radical wherein each cyclic moiety has about 3 to about 8 carbon atoms. Examples of cycloalkyl radicals include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like.

The term "cycloalkylalkyl" refers to an alkyl radical as defined above which is substituted by a cycloalkyl radical having from about 3 to about 8 carbon atoms.

The term "aralkyl" refers to an alkyl radical as defined above in which one hydrogen atom is replaced by an aryl radical as defined above, such as, for example, benzyl, 2-phenylethyl and the like.

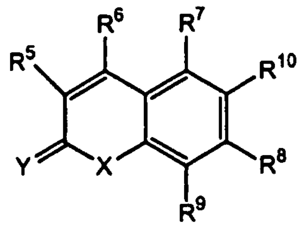
The terms alkyl, alkenyl, and alkynyl include optionally substituted straight-chain, branched-chain, cyclic, saturated and/or unsaturated structures, and combinations thereof.

The terms haloalkyl, haloalkenyl and haloalkynyl include alkyl, alkenyl and alkynyl structures, as described above, that are substituted with one or more fluorines, chlorines, bromines or iodines, or with combinations thereof.

The terms heteroalkyl, heteroalkenyl and heteroalkynyl include optionally substituted alkyl, alkenyl and alkynyl structures, as described above, in which one or more skeletal atoms are oxygen, nitrogen, sulfur, or combinations thereof.

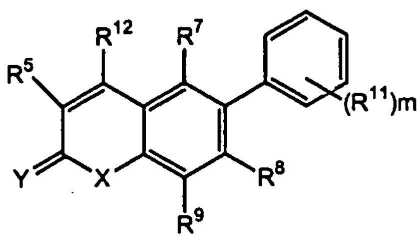
The substituents of an "optionally substituted" structure include, for example, one or more, preferably 1 to 4, more preferably 1 to 2 of the following preferred substituents: alkyl, alkenyl, alkynyl, aryl, heteroaryl, alkoxy, aryloxy, cycloalkyl, cycloalkylalkyl, arylalkyl, amino, alkylamino, dialkylamino, F, Cl, Br, I, CN, NO_2, NH_2, $NHCH_3$, $N(CH_3)_2$, SH, SCH_3, OH, OCH_3, OCF_3, CH_3, CF_3, $C(O)CH_3$, CO_2CH_3, CO_2H and $C(O)NH_2$.

Examples of compounds of the present invention are represented by those having the formula:



(I)

OR



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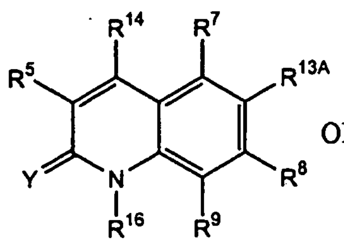

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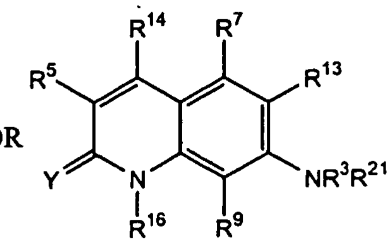

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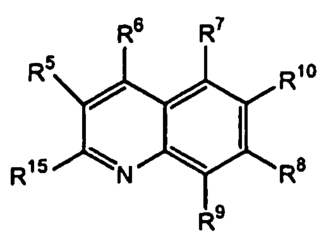
OR



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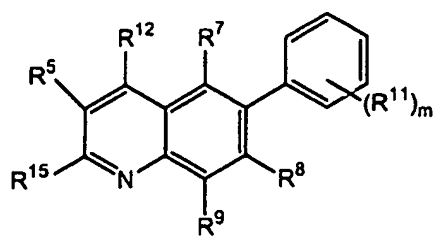

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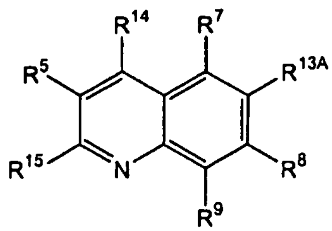
OR



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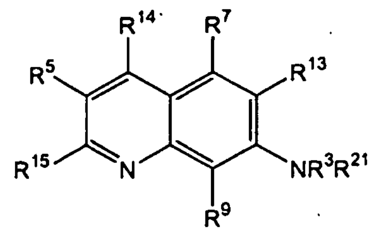

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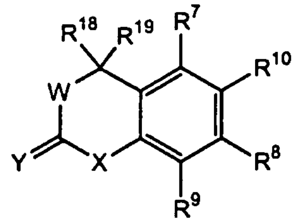
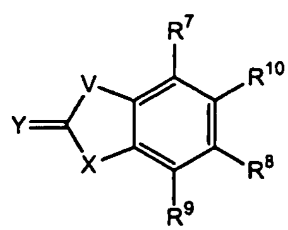
OR



(VII)

OR



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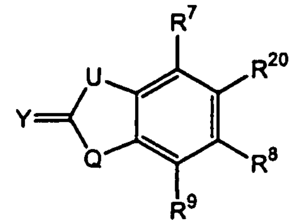


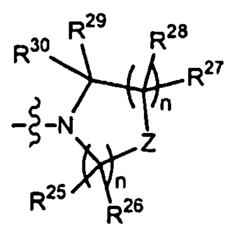
(IX)

wherein:

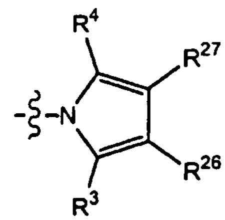
R^1 and R^2 each independently represent COR^3, CSR^3, SO_2R^3, NO, NR^3R^4, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_2-C_8 haloalkynyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl, C_2-C_8 heteroalkynyl, $(CH_2)_nR^3$, aryl, or heteroaryl and wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, aryl, and heteroaryl may be optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, SR^3, SOR^3, SO_2R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl, or alternatively,

R^1 and R^2 may be taken together to form a three- to nine-membered alkyl, alkenyl, heteroalkyl, or heteroalkenyl ring and wherein the alkyl, alkenyl, heteroalkyl, or heteroalkenyl ring may be optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl, or

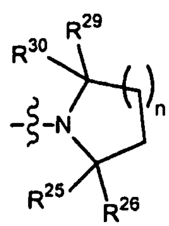
R^1 and R^2 may be taken together to form one of:



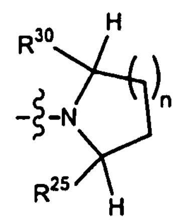
or



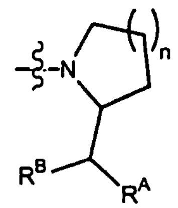
Preferably, R^1 and R^2 may be taken together to form:



More preferably, R^1 and R^2 may be taken together to form:



Most preferably, R^1 and R^2 may be taken together to form:



R^A represents hydrogen, OR^C, O_2CR^C, $(CH_2)_nOR^C$, NHR^C, $NHCOR^C$, F, Cl, Br, I, CN, SCN, SCH_3;

R^B represents hydrogen, F, Cl, Br, I, CHF_2, CF_3, C_1-C_6 alkyl, aryl, heteroaryl, wherein the alkyl, aryl and heteroaryl may be optionally substituted with F, Cl, Br, I, CN, NO_2, OH, OCH_3, CF_3, C_1-C_6 alkyl;

R^C represents hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, $(CH_2)_nR^D$;

R^D represents aryl or heteroary, optionally substituted with F, Cl, Br, I, CN, NO_2, OH, OCH_3, CF_3, C_1-C_6 alkyl;

R^3 and R^4 each independently represent hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, heteroaryl, or aryl and wherein the alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, heteroaryl, and aryl may be optionally substituted with halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^5 represents hydrogen, F, Cl, Br, I, OR^3, SR^3, SOR^3, SO_2R^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

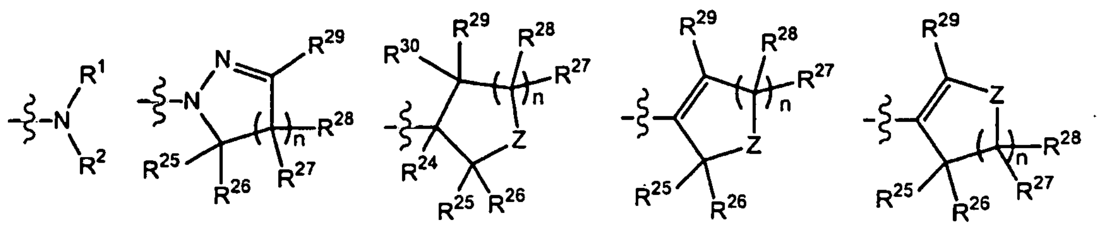
R^6 represents F, Cl, Br, I, CH_3, CF_3, CHF_2, CFH_2, CN, CF_2Cl, CF_2OR^3, OR^3, SR^3, SOR^3, SO_2R^3, NR^3R^4, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_4 haloalkyl, C_2-C_4 haloalkenyl, C_2-C_4 haloalkynyl, C_1-C_4 heteroalkyl, C_2-C_4 heteroalkenyl, or C_2-C_4 heteroalkynyl and wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl,

heteroalkynyl, aryl, and heteroaryl may be optionally substituted with halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^7 and R^8 each independently represent hydrogen, F, Cl, Br, I, CN, OR^3, NR^3R^4, $NR^3CR^3R^4CONR^3R^4$, $C_n(R^3)_{2n}OR^3$, SR^3, SOR^3, SO_2R^3, NR^3COR^4, C_1-C_8 alkyl, C_1-C_8 haloalkyl, or C_1-C_8 heteroalkyl;

R^9 represents hydrogen, F, Br, Cl, I, OR^3, NR^3R^4, SR^3, SOR^3, SO_2R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^{10} represents one of:



R^{11} represents hydrogen, F, Br, Cl, I, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, NO_2, CN, CF_3, OR^3, NR^3R^4, SR^3, SOR^3, or SO_2R^3;

R^{12} is F, Br, Cl, I, CN, OR^3, SR^3, SOR^3, SO_2R^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^{13} represents hydrogen, F, Cl, Br, I, CN, OR^1, NHR^1, COR^3, CO_2R^3, SR^1, SOR^3, SO_2R^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_2-C_8 haloalkynyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl, C_2-C_8 heteroalkynyl, $(CH_2)_nR^3$, or heteroaryl and wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, $(CH_2)_nR^3$, and heteroaryl may be optionally substituted with F, Cl, Br, I, CN, NO_2, NR^1R^3, SR^1, SOR^3, SO_2R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^{14} represents F, Br, Cl, I, CF_3, CHF_2, CH_2F, CF_2Cl, or CF_2OR^3;

R^{15} represents hydrogen, F, Br, Cl, I, CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, OR^{16}, $NR^{16}R^4$, SR^{16}, CH_2R^{16}, COR^3, CO_2R^3, $CONR^3R^4$, SOR^3, or SO_2R^3;

R^{16} represents hydrogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, aryl, heteroaryl, COR^{17}, CO_2R^{17}, or $CONR^{17}R^{17}$;

R^{17} represents hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^{18} and R^{19} each independently represent hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 heteroalkyl, or alternatively, R^{18} and R^{19} may be taken together to form a three- to seven-membered ring;

R^{20} represents an aryl or heteroaryl wherein the aryl or heteroaryl may be optionally substituted with F, Cl, Br, CN, OR^1, SR^1, SOR^3, SO_2R^3, NO_2, NR^1R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^{21} represents $CR^3R^4CONR^3R^4$, $C_n(R^3)_{2n}OR^3$, SOR^3, SO_2R^3, C_2-C_8 alkyl, C_2-C_8 haloalkyl, and C_2-C_8 heteroalkyl;

R^{22} and R^{23} each independently represent hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 heteroalkyl, or alternatively R^{22} and R^{23} may be taken together to form a three- to seven-membered ring;

R^{24} represents hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, or OR^3;

R^{25} through R^{30} each independently represent hydrogen, F, Cl, Br, I, OR^3, NR^3R^4, SR^3, SOR^3, SO_2R^3, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkynyl or C_2-C_6 alkenyl, and wherein the alkyl, haloalkyl, heteroalkyl, alkynyl, and alkenyl may be optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, aryl or heteroaryl and wherein the aryl and heteroaryl may be optionally substituted with F, Cl, Br, I, CN, NO_2, OH, OCH_3, CF_3 or C_1-C_6 alkyl;

Any two of R^{25} through R^{30} when taken together can form a three to seven-membered alkyl or alkenyl or heteroalkyl ring; or any four of R^{25} through R^{30} when taken together can form a fused aromatic ring;

Q represents O or S;

U represents V, $OCR^{22}R^{23}$, $SCR^{22}R^{23}$, $NR^3CR^{22}R^{23}$, $CR^3R^4CR^{22}R^{23}$;

V represents O, S, NR^3, $CR^{22}R^{23}$, CR^3R^4O, or CR^3R^4S, but, V is not S when R^1 and R^2 are both methyl;

W represents O, S, NR^3, $CR^{25}R^{26}$;

X represents O, S or NR^{16};

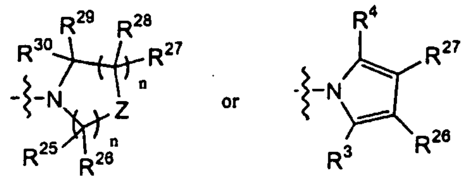
Y represents O, S, NR^3, NOR^3 or CR^3R^4;

Z represents O, S, NR^3, C=O, or CR^3R^4, or optionally Z may represent two hydrogens;

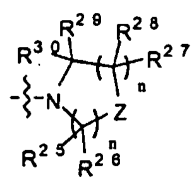
n is 1, 2, 3 or 4; and

m is 1 to 5.

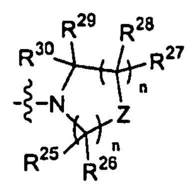
Preferred R^1 and R^2 groups include COR^3, CSR^3, SO_2R^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl, $(CH_2)_nR^{3A}$, aryl, and heteroaryl, wherein the aryl, or heteroaryl may be optionally substituted with F, Cl, Br, OR^3, NR^3R^4, CN, NO_2, SR^3, COMe, $COCF_3$, C_1-C_4 alkyl, C_1-C_4 haloalkyl. Also preferred, R^1 and R^2 groups may be taken together to form one of:



More preferred R^1 and R^2 groups include COR^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_1-C_8 heteroalkyl, CH_2R^{3A}, aryl and heteroaryl. The aryl or heteroaryl may be optionally substituted with F, Cl, Br, OH, OMe, SH, SMe, CN, NO_2, CF_3, Me, COMe, or R^1 and R^2 groups may be taken together to form:



Most preferably, R^1 and R^2 groups include C_1-C_8 alkyl, C_2-C_8 alkenyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, and CH_2R^{3A}, or, R^1 and R^2 groups may be taken together to form:



Preferred R^3 and R^4 groups include hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_1-C_8 haloalkyl, and C_1-C_8 heteroalkyl. More preferred R^3 and R^4 groups include hydrogen, C_1-C_6

alkyl and C_1-C_8 haloalkyl. Most preferably, R^3 and R^4 each independently is selected from group of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl.

Preferred R^{3A} groups include aryl and heteroaryl, wherein the aryl and heteroaryl may be optionally substituted with halogen, CN, OMe, SMe, C_1-C_4 alkyl, or C_1-C_4 haloalkyl. More preferred R^{3A} groups include heteroaryl and aryl, wherein the heteroaryl and aryl may be optionally substituted with F, Cl, Br, CN, OMe, C_1-C_4 alkyl, or C_1-C_4 haloalkyl. Most preferably, R^{3A} groups include heteroaryl and aryl, wherein the heteroaryl and aryl may be optionally substituted with F, Cl, Br, CN, CF_3, OMe, or C_1-C_4 alkyl.

Preferred R^5 groups include hydrogen, F, Cl, Br, OH, OMe, C_1-C_4 alkyl, and C_1-C_4 haloalkyl. More preferred R^5 groups include hydrogen, F, Cl, OH, OMe, C_1-C_4 alkyl, and CF_3. Most preferred R^5 groups include hydrogen, F, Cl, OH, and OMe.

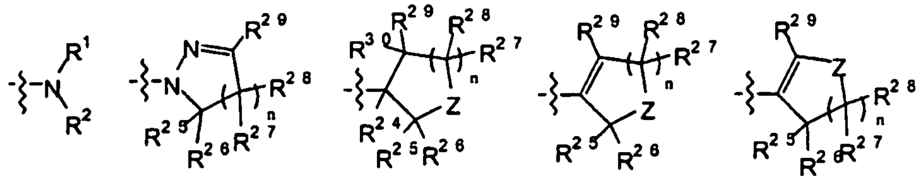
Preferred R^6 groups include F, Cl, Br, CH_3, CF_3, CHF_2, CFH_2, CN, CF_2Cl, CF_2OR^3, OR^3, SR^3, NR^3R^4, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 haloalkyl, C_2-C_4 haloalkenyl, C_1-C_4 heteroalkyl, and C_2-C_4 heteroalkenyl. More preferred R^6 groups include F, Cl, Br, CF_3, CHF_2, CFH_2, CN, CF_2Cl, CF_2OMe, and C_1-C_4 alkyl. Most preferred R^6 groups include F, Cl, C_1-C_4 alkyl, CF_3, CHF_2, CFH_2, CF_2Cl, CF_2OMe, and OMe.

Preferred R^7 groups include hydrogen, F, Cl, Br, OR^3, NR^3R^4, SR^3, C_1-C_8 alkyl, C_1-C_8 haloalkyl, or C_1-C_8 heteroalkyl. More preferred R^7 groups include hydrogen, F, Cl, Me, OMe, and CF_3. Most preferred R^7 groups include hydrogen, F, Cl, Me, and OMe.

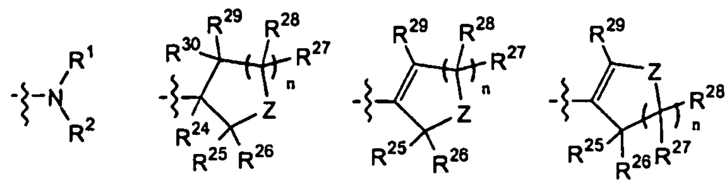
Preferred R^8 groups include hydrogen, F, Cl, Br, OR^3, NR^3R^4, SR^3, C_1-C_8 alkyl, C_1-C_8 haloalkyl, and C_1-C_8 heteroalkyl. More preferred R^8 groups include hydrogen, F, Cl, Br, OR^3, NR^3R^4, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkyl. Most preferred R^8 groups include hydrogen, F, Cl, Br, OR^3, NR^3R^4, C_1-C_6 alkyl, C_1-C_6 haloalkyl.

Preferred R^9 groups include hydrogen, F, Br, Cl, OR^3, NR^3R^4, SR^3, C_1-C_4 alkyl, and C_1-C_4 haloalkyl. More preferred R^9 groups include hydrogen, F, Br, OH, Me, OMe, and CF_3. Most preferred R^9 groups include hydrogen, F, Cl, OH, Me, OMe, and CF_3.

Preferred R^{10} groups include:



More preferred R^{10} groups include:



Preferred R^{11} groups include F, Br, Cl, I, C_1-C_6 alkyl, C_1-C_6 haloalkyl, NO_2, CN, CF_3, OH, OMe, NR^3R^4, and SR^3. More preferred R^{11} groups include F, Br, Cl, C_1-C_6 alkyl, NO_2, CN, CF_3, OH, OMe.

Preferred R^{12} groups include F, Br, Cl, and C_1-C_4 haloalkyl. More preferred R^{12} groups include F, Br, Cl, CF_3, CF_2H and CFH_2.

Preferred R^{13} groups include hydrogen, F, Cl, Br, I, CN, OR^3, NR^3R^4, SR^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_2-C_8 haloalkynyl, C_1-C_8 heteroalkyl, and $(CH_2)_nR^{3A}$. More preferred R^{13} groups include hydrogen, F, Cl, Br, OR^3, SR^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_1-C_8 haloalkyl. Most preferred R^{13} groups include hydrogen, F, Cl, Br, C_1-C_4 alkyl, C_2-C_4 alkenyl, or C_1-C_8 haloalkyl.

Preferred R^{13A} groups include NHR^1 or heteroaryl, wherein the heteroaryl may be optionally substituted with F, Cl, Br, CN, NMe_2, NO_2, CF_3, Me or OMe. More preferred R^{13A} is NHR^1.

Preferred R^{14} groups include F, Br, Cl, CF_3, CHF_2, CH_2F, CF_2Cl, and CF_2OMe. More preferred R^{14} groups include F, Cl, CF_3, CHF_2, CH_2F, and CF_2Cl. Most preferred R^{14} groups include Cl, CF_3, CHF_2, CH_2F, and CF_2Cl.

Preferred R^{15} groups include F, Br, Cl, CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, OR^{16}, $NR^{16}R^4$, and SR^{16}. More preferred R^{15} groups include F, Cl, CN, OR^{16}, and SR^{16}. Most preferred R^{15} groups include Cl, OR^{16}, $NR^{16}R^4$ and SR^{16}.

Preferred R^{16} groups include hydrogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, COR^{17}, CO_2R^{17}, and $CONR^{17}R^{17}$. More preferred R^{16} groups include hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, COR^{17}, CO_2R^{17}, and $CONR^{17}R^{17}$. Most preferred R^{16} groups include hydrogen, C_1-C_6 alkyl, COR^{17}, CO_2R^{17}, and $CONR^{17}R^{17}$.

Preferred R^{17} groups include C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 heteroalkyl.

Preferred R^{18} and R^{19} groups include C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl and R^{18} and R^{19} may be taken together to form a four- to seven-membered ring. More preferred R^{18} and R^{19} groups include C_1-C_6 alkyl, and C_1-C_6 haloalkyl and R^{18} and R^{19} may be taken together to form a five- to six-membered ring. Most preferred R^{18} and R^{19} groups include C_1-C_4 alkyl, C_1-C_4 haloalkyl and R^{18} and R^{19} may be taken together to form a five- to six-membered ring.

Preferred R^{20} groups include aryl and heteroaryl. The aryl or heteroaryl may be optionally substituted with F, Cl, Br, CN, NO_2, CF_3 and C_1-C_4 alkyl.

Preferred R^{21} groups include C_2-C_8 alkyl, C_2-C_8 haloalkyl, and C_2-C_8 heteroalkyl. More preferred R^{21} groups include C_2-C_8 alkyl, and C_2-C_8 haloalkyl.

Preferred R^{22} and R^{23} groups include hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkyl and R^{22} and R^{23} groups may be taken together to form a three- to seven-membered ring. More preferred R^{22} and R^{23} groups include hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and R^{22} and R^{23} groups taken together to form a four- to six-membered ring.

Preferred R^{24} groups include hydrogen and OR^3. More preferred R^{24} groups include hydrogen and OH.

Preferred R^{25}, R^{26}, R^{27}, R^{28}, R^{29} and R^{30} groups include hydrogen, F, Cl, Br, OR^3, NR^3R^4, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, and C_2-C_6 alkenyl, wherein the alkyl, haloalkyl, heteroalkyl, alkynyl, or alkenyl may be optionally substituted with F, Cl, Br, OR^3, NR^3R^4, aryl or heteroaryl and the aryl and heteroaryl may be optionally substituted with F, Cl, Br, CN, NO_2, OH, OCH_3, CF_3 or C_1-C_6 alkyl. Also preferred is any two of R^{25}, R^{26}, R^{27}, R^{28}, R^{29} and R^{30} groups taken together to form a three- to seven-membered alkyl or alkenyl or heteroalkyl ring. Also preferred is any four of R^{25}, R^{26}, R^{27}, R^{28}, R^{29} and R^{30} groups taken together to form a fused aromatic ring. More preferred R^{25} through R^{30} groups include hydrogen, F, Cl, OH, OMe, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl and C_2-C_6 alkenyl. Also more preferred is any two of R^{25}, R^{26}, R^{27}, R^{28}, R^{29} and R^{30} groups taken together to form a four to six-membered alkyl or

alkenyl ring. Also more preferred is any four of R^{25}, R^{26}, R^{27}, R^{28}, R^{29} and R^{30} groups taken together to form a fused aromatic ring. Most preferred R^{25} through R^{30} groups include hydrogen, F, Cl, OH, OMe, C_1-C_4 alkyl, and C_1-C_4 haloalkyl.

Preferably Q is O.

Preferred U groups include V, $OCR^{22}R^{23}$, $NR^3CR^{22}R^{23}$, $CR^3R^4CR^{22}R^{23}$.

Preferred V groups include $CR^{22}R^{23}$, CR^3R^4O, and CR^3R^4S.

Preferred W groups include O, NR^3, and CR^3R^4. More preferred W groups include O, and CR^3R^4. Most preferably, W is O.

Preferred X groups include S and NR^{16}. More preferred X groups include O and NR^{16}. Most preferably, X is NR^{16}.

Preferred Y groups include O, S, NR^3, and NOR^3. More preferred Y groups include O, S, and NOR^3. Most preferably, Y is O or S.

Preferred Z groups include O, S, NR^3, $CR^{25}R^{26}$ and two hydrogens. More preferred Z groups include O, $CR^{25}R^{26}$ and two hydrogens. Most preferably, Z groups include O, CR^3R^4 and two hydrogens.

Preferably, n is 1 or 2.

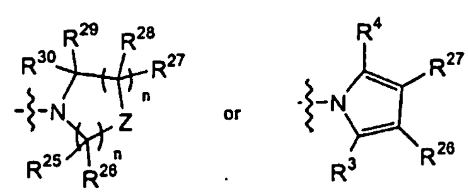
Preferably, m is 1 to 4. More preferably, m is 1 to 3.

In a preferred embodiment of the invention, R^1 and R^2 are each independently selected from the group of COR^3, CSR^3, SO_2R^3, NO, NR^3R^4, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_2-C_8 haloalkynyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl, C_2-C_8 heteroalkynyl, $(CH_2)_nR^{3A}$, aryl, and heteroaryl, wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, aryl, and heteroaryl are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, CN, NO_2, SR^3, SOR^3, SO_2R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl. R^3 and R^4 are each independently hydrogen or optionally substituted C_1–C_6 alkyl. R^{3A} is optionally substituted alkyl or heteroaryl. R^5 is selected from the group of hydrogen, halogen and optionally substituted C_1–C_6 alkyl. R^7 and R^8 are each independently hydrogen or halogen; and R^9 is hydrogen or halogen. R^{11} is selected from the group of halogen, CN, $N0_2$ and optionally substituted C_1 - C_6 haloalkyl. R^{12} is halogen or optionally substituted haloalkyl. R^{13} is selected from the group of hydrogen C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl, wherein said C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl are optionally substituted.

R^{15} is halogen or OR^{16}. R^{18} and R^{19} are each independently optionally substituted $C_1 - C_6$ alkyl; or R^{18} and R^{19} taken together form a five- to six-membered ring. R^{22} and R^{23} are each independently hydrogen or optionally substituted $C_1 - C_6$ alkyl; or R^{22} and R^{23} together form a three- to seven-membered ring. R^{25} through R^{30} are each independently hydrogen, $C_1 - C_6$ alkyl, or $C_1 - C_6$ haloalkyl, wherein said $C_1 - C_6$ alkyl and $C_1 - C_6$ haloalkyl are optionally substituted; Y is selected from the group of O, S, and NR^3; and m is 1 to 3.

In another preferred embodiment of the invention R^1 and R^2 taken together form a three- to nine-membered alkyl, alkenyl, heteroalkyl, or heteroalkenyl ring, wherein the alkyl, alkenyl, heteroalkyl, or heteroalkenyl ring are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl. R^3 and R^4 are each independently hydrogen or optionally substituted C_1–C_6 alkyl. R^{3A} is optionally substituted alkyl or heteroaryl. R^5 is selected from the group of hydrogen, halogen and optionally substituted C_1–C_6 alkyl. R^7 and R^8 are each independently hydrogen or halogen. R^9 is hydrogen or halogen. R^{11} is selected form the group of halogen, CN, NO_2 and optionally substituted $C_1 - C_6$ haloalkyl. R^{12} is halogen or optionally substituted haloalkyl. R^{13} is selected from the group of hydrogen, $C_1 - C_6$ alkyl and $C_1 - C_6$ heteroalkyl, wherein said $C_1 - C_6$ alkyl and $C_1 - C_6$ heteroalkyl are optionally substituted. R^{15} is halogen or OR^{16}. R^{18} and R^{19} are each independently optionally substituted $C_1 - C_6$ alkyl; or R^{18} and R^{19} taken together form a five- to six-membered ring. R^{22} and R^{23} are each independently hydrogen or optionally substituted $C_1 - C_6$ alkyl; or R^{22} and R^{23} together form a three- to seven-membered ring. R^{25} through R^{30} are each independently hydrogen, $C_1 - C_6$ alkyl, or $C_1 - C_6$ haloalkyl, wherein said $C_1 - C_6$ alkyl and $C_1 - C_6$ haloalkyl are optionally substituted. Y is selected from the group of O, S, and NR^3; and m is 1 to 3.

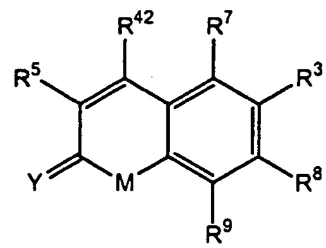
In still another preferred embodiment of the invention, R^1 and R^2 taken together form one of:



R^3 and R^4 are each independently hydrogen or optionally substituted C_1–C_6 alkyl. R^{3A} is optionally substituted alkyl or heteroaryl. R^5 is selected from the group of hydrogen, halogen

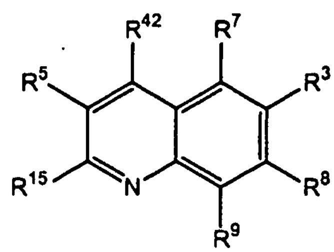
and optionally substituted C_1–C_6 alkyl. R^7 and R^8 are each independently hydrogen or halogen. R^9 is hydrogen or halogen. R^{11} is selected form the group of halogen, CN, NO_2 and optionally substituted C_1 - C_6 haloalkyl. R^{12} is halogen or optionally substituted haloalkyl. R^{13} is selected from the group of hydrogen C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl, wherein said C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl are optionally substituted. R^{15} is halogen or OR^{16}. R^{18} and R^{19} are each independently optionally substituted C_1 - C_6 alkyl; or R^{18} and R^{19} taken together form a five- to six-membered ring. R^{22} and R^{23} are each independently hydrogen or optionally substituted C_1 - C_6 alkyl; or R^{22} and R^{23} together form a three- to seven-membered ring. R^{25} through R^{30} are each independently hydrogen, C_1 - C_6 alkyl, or C_1 - C_6 haloalkyl, wherein said C_1 - C_6 alkyl and C_1 - C_6 haloalkyl are optionally substituted; Y is selected from the group of O, S, and NR^3; and m is 1 to 3.

The present invention further provides methods of modulating processes mediated by AR or PR or combinations thereof comprising administering to a patient an effective amount of a pharmaceutical composition of the present invention comprising one or more compounds represented by those having the following formulas as well as pharmaceutical compositions of the above compounds:



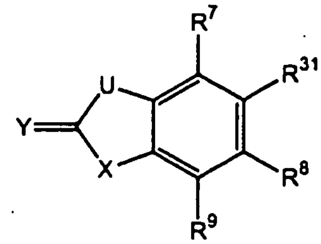
(X)

OR



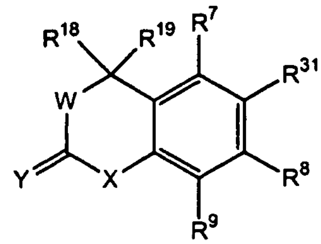
(XI)

OR



(XII)

OR



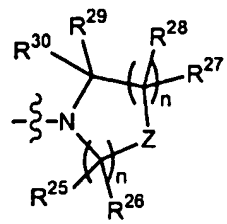
(XIII)

wherein:

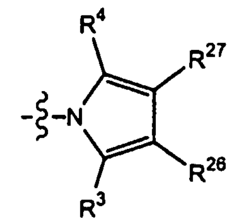
R^1 and R^2 each independently represent COR^3, CSR^3, SO_2R^3, NO, NR^3R^4, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_2-C_8 haloalkynyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl, C_2-C_8 heteroalkynyl, $(CH_2)_nR^3$, aryl, or heteroaryl and wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, aryl, and heteroaryl may be optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, SR^3, SOR^3, SO_2R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl, or alternatively,

R^1 and R^2 may be taken together to form a three- to nine-membered alkyl, alkenyl, heteroalkyl, or heteroalkenyl ring and wherein the alkyl, alkenyl, heteroalkyl, and heteroalkenyl ring may be optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl, or

R^1 and R^2 may be taken together to form one of:



or



R^3 and R^4 each independently represent hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, heteroaryl, or aryl and wherein the alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, heteroaryl, and aryl may be optionally substituted with halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^5 represents hydrogen, F, Cl, Br, I, OR^3, SR^3, SOR^3, SO_2R^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^7 and R^8 each independently represent hydrogen, F, Cl, Br, I, CN, OR^3, NR^3R^4, $NR^3CR^3R^4CONR^3R^4$, $C_n(R^3)_{2n}OR^3$, SR^3, SOR^3, SO_2R^3, NR^3COR^4, C_1-C_8 alkyl, C_1-C_8 haloalkyl, or C_1-C_8 heteroalkyl;

R^9 represents hydrogen, F, Br, Cl, I, OR^3, NR^3R^4, SR^3, a C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^{11} represents hydrogen, F, Br, Cl, I, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, NO_2, CN, CF_3, OR^3, NR^3R^4, SR^3, SOR^3, or SO_2R^3;

R^{15} represents hydrogen, F, Br, Cl, I, CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, OR^{16}, $NR^{16}R^4$, SR^{16}, CH_2R^{16}, COR^3, CO_2R^3, $CONR^3R^4$, SOR^3, or SO_2R^3;

R^{16} represents hydrogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, aryl, heteroaryl, COR^{17}, CO_2R^{17}, or $CONR^{17}R^{17}$;

R^{17} represents hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^{18} and R^{19} each independently represent hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 heteroalkyl, or alternatively, R^{18} and R^{19} may be taken together to form a three- to seven-membered ring;

R^{22} and R^{23} each independently represent hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 heteroalkyl, or alternatively, R^{22} and R^{23} may be taken together to form a three- to seven-membered ring;

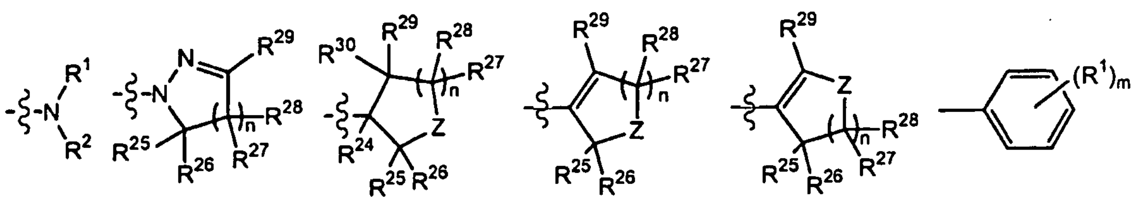
R^{24} represents hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, or OR^3;

R^{25} through R^{30} each independently represent hydrogen, F, Cl, Br, I, OR^3, NR^3R^4, SR^3, SOR^3, SO_2R^3, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkynyl or C_2-C_6 alkenyl, and wherein the alkyl, haloalkyl, heteroalkyl, alkynyl, and alkenyl may be optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, aryl or heteroaryl and wherein the aryl and heteroaryl may be optionally substituted with F, Cl, Br, I, CN, NO_2, OH, OCH_3, CF_3 or C_1-C_6 alkyl;

Any two Rs of R^{25} through R^{30} when taken together can form a three to seven-membered alkyl or alkenyl or heteroalkyl ring; or any four Rs of R^{25} through R^{30} when taken together can form a fused aromatic ring;

R^{31} represents hydrogen, F, Cl, Br, I, CN, OR^1, NHR^1, COR^3, CO_2R^3, SR^1, SOR^3, SO_2R^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl, C_2-C_8 alkynyl, C_2-C_8 haloalkynyl, C_2-C_8 heteroalkynyl, $(CH_2)_nR^3$ or heteroaryl and wherein the alkyl, alkenyl, haloalkyl, haloalkenyl, heteroalkyl, heteroalkenyl, allyl, alkynyl, haloallyl, haloalkynyl, heteroalkynyl, $(CH_2)_nR^3$, and heteroaryl may be optionally substituted with F, Cl, Br, I, CN, OR^1, NO_2, NR^1R^3, SR^1, SOR^3, SO_2R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl, or C_1-C_4 heteroalkyl or optionally,

R^{31} represents one of:



R^{42} represents hydrogen, F, Cl, Br, I, CH_3, CF_3, CHF_2, CFH_2, CN, CF_2Cl, CF_2OR^3, OR^3, SR^3, SOR^3, SO_2R^3, NR^3R^4, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_4 haloalkyl, C_2-C_4 haloalkenyl, C_2-C_4 haloalkynyl, C_1-C_4 heteroalkyl, C_2-C_4 heteroalkenyl, or C_2-C_4 heteroalkynyl, and wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, aryl, and heteroaryl may be optionally substituted with halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

M represents O, S, NR^{16};

U represents O, S, NR^3, $CR^{22}R^{23}$, CR^3R^4O, or CR^3R^4S;

W represents O, S, NR^3, $CR^{22}R^{23}$;

X represents O, S or NR^{16}, but when R^{31} is an aryl or heteroaryl, X is not NR^{16};
Y represents O, S, NR^{16}, NOR^{16} or $CR^{16}R^{17}$;
Z represents O, S, NR^3, C=O, or CR^3R^4, or optionally Z may represent two hydrogens;
n is 1, 2 or 3; and
m is 1 to 5.

In a preferred aspect, the present invention provides a pharmaceutical composition comprising an effective amount of an AR or PR modulating compound of formulas I through XIII shown above wherein R^1 through R^{42}, M, Q, U, V, W, X, Y and Z all have the same definitions as given above.

In a further preferred aspect, the present invention comprises a method of modulating processes mediated by ARs or PRs or combinations comprising administering to a patient an effective amount of a compound of the formulae I through XIII shown above wherein R^1 through R^{42}, M, Q, U, V, W, X, Y and Z all have the same definitions as given above.

Any of the compounds of the present invention can be synthesized as pharmaceutically acceptable salts for incorporation into various pharmaceutical compositions. As used herein, pharmaceutically acceptable salts include, but are not limited to, hydrochloric, hydrobromic, hydroiodic, hydrofluoric, sulfuric, citric, maleic, acetic, lactic, nicotinic, succinic, oxalic, phosphoric, malonic, salicylic, phenylacetic, stearic, pyridine, ammonium, piperazine, diethylamine, nicotinamide, formic, urea, sodium, potassium, calcium, magnesium, zinc, lithium, cinnamic, methylamino, methanesulfonic, picric, tartaric, triethylamino, dimethylamino, and tris(hydroxymethyl)aminomethane. Additional pharmaceutically acceptable salts are known to those skilled in the art.

AR agonist, partial agonist and antagonist compounds (including compounds with tissue-selective AR modulator activity) of the present invention are useful in the treatment of hypogonadism (agonist), male hormone replacement therapy (agonist), wasting diseases (agonist), cancer cachexia (agonist), male contraception, hirsutism (antagonist), stimulation of hematopoiesis (agonist), acne (antagonist), male-pattern baldness (antagonist), prostatic hyperplasia (antagonist), various hormone-dependent cancers, including, without limitation, prostate (antagonist),and breast cancer and as anabolic agents (agonist). It is understood by those of skill in the art that a partial agonist may be used where agonist activity is desired, or where

antagonist activity is desired, depending upon the AR modulator profile of the particular pa agonist.

PR agonist, partial agonist and antagonist compounds of the present invention are useful in female hormone replacement therapy and as modulators of fertility (e.g., as contraceptives, contragestational agents or abortifacients), either alone or in junction with ER modulators. The PR modulators are also useful in the treatment of dysfunctional uterine bleeding, dysmenorrhea, endometriosis, leiomyomas (uterine fibroids), hot flashes, mood disorders, meningiomas as well as in various hormone-dependent cancers, including, without limitation, cancers of ovary, breast, endometrium and prostate.

It is understood by those skilled in the art that although the compounds of the present invention are typically employed as selective agonists, partial agonists or antagonists, there may be instances where a compound with a mixed steroid receptor profile is preferred.

Furthermore, it is understood by those skilled in the art that the compounds of the present invention, including pharmaceutical compositions and formulations containing these compounds, can be used in a wide variety of combination therapies to treat the conditions and diseases described above. Thus, the compounds of the present invention can be used in combination with other hormones and other therapies, including, without limitation, chemotherapeutic agents such as cytostatic and cytotoxic agents, immunological modifiers such as interferons, interleukins, growth hormones and other cytokines, hormone therapies, surgery and radiation therapy.

Representative AR modulator compounds (i.e., agonists and antagonists) according to the present invention include:

6-Amino-4-trifluoromethyl-2(*1H*)-quinolinone (Compound **200**);

6-Propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **204**);

6-Isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **205**);

6-Isobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **206**);

6-(2,2-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **207**);

6-Cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **208**);

6-(2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **209**);

6-(2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **210**);

6-(2,2-Difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **211**);

6-(2-Chloro-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **212**);

6-Acetylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **213**);

6-Trifluoroacetylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **214**);

6-Benzoylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **215**);

6-Dimethylacetylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **216**);

6-Dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **217**);

6-Diethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **218**);

6-Dipropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **219**);

6-Dibutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **220**);

6-Diisobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **221**);

6-(bis-Cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **222**);

6-(bis-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **223**);

6-(bis-2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **224**);

6-(bis-2-Chloro-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **225**);

6-(bis-2-Bromoethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **226**);

6-(N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **227**);

6-(bis-N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **228**);

6-(N-2,2,2-Chlorodifluoroethyl-N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **229**);

6-(bis-N-2,2-Difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **230**);

6-(N-2,2-Dichloroethyl-N-2,2,2-trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **231**);

6-(bis-N-2,2-Dichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **232**);

6-(N-2,2-Dichloroethyl-N-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **233**);

6-(N-2,2-Dichloroethyl-N-2,2,2-chlorodifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **234**);

6-(N-Isopropyl-N-methyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **235**);

6-(N-Methyl-N-cyclopentyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **236**);

6-(N-Methyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **237**);

6-(N-Ethyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **238**);

6-(N-Ethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **239**);

6-(N-Ethyl-N-1-methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **240**);

6-(N-Ethyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **241**);

6-(N-Ethyl-N-2,2-dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **242**);

6-(N-Ethyl-N-cyclopentyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **243**);

6-(N-Ethyl-N-1-acetylethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **244**);

(±)-6-(N-Ethyl-N-1-methyl-2-hydroxypropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **245**);

6-(N-Ethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **246**);

6-(N-Ethyl-N-3-furylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **247**);

(±)-6-(N-Ethyl-N-2,2-dimethoxyisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **248**);

6-(N-Isopropyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **249**);

6-(N-2-Hydroxyethyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **250**);

(±)-6-(N-Propyl-N-1-methylbutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **251**);

(±)-6-(N-Propyl-N-1,2-dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **252**);

6-(N-Propyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **253**);

6-(N-Propyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **254**);

(±)-6-(N-Propyl-N-1-methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **255**);

6-(N-2-Hydroxyethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **256**);

6-(N-Isopropyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **257**);

6-(N-Methyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **258**);

6-(N-2,2,2-trifluoroethyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **259**);

6-(N-2,2,2-trifluoroethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **260**);

6-(N-2,2,2-Trifluoroethyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **261**);

(±)-6-(N-2,2,2-Trifluoroethyl-N-1-methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **262**);

(±)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **263**);

(+)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **264**);

(-)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **265**);

6-(N-2,2,2-Trifluoroethyl-N-3-furfuryl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **266**);

6-(N-2,2,2-Trifluoroethyl-N-3-thiophenemethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **267**);

6-(N-2,2,2-Trifluoroethyl-N-3,3-dimethylbutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **268**);

6-(N-2,2,2-Trifluoroethyl-N-2-thiophenemethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **269**);

6-(N-2,2,2-Trifluoroethyl-N-2-furfuryl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **270**);

6-(N-Butyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **271**);

6-(bis-N,N-Benzyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **272**);

6-(N-2,2,2-Trifluoroethyl-N-cyclobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **273**);

6-(N-2,2,2-Trifluoroethyl-N-2,2-dichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **274**);

6-(N-2,2,2-Trifluoroethyl-N-2-chloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **275**);

6-(N-Benzyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **276**);

6-(N-4-Fluorobenzyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **277**);

6-(N-Propyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **278**);

6-(N-2,2,3,3,3-Pentafluoropropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **279**);

6-Diallylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **280**);

6-(N-Isobutyl-N-allyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **281**);

6-(N-Isopropyl-N-allyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **282**);

6-(N-Allyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **283**);

6-Allylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **284**);

6-(N-Allyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **285**);

6-(N-Allyl-N-2,2,2-trifluoroacetyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **286**);

6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroacetyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **287**);

6-(N-Allyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **288**);

(±)-6-(N-2-Hydroxyisopropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **289**);

(±)-6-(N-Isobutyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **290**);

6-(N-2,2-Difluoroethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **291**);

6-(N-2,2-Dimethylpropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **292**);

6-(N-2,2-Difluoro-2-chloroethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **293**);

6-(N-2,2-Difluoro-2-chloroethyl-N-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **294**);

6-(N-2,2,2-Trifluoroethyl-N-methylsufonyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **295**);

1-Methyl-6-(N-propyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **296**);

1-Methyl-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **297**);

1-Ethyl-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **298**);

6-(N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **299**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **300**);

(±)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **301**);

(+)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **302**);

(-)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **303**);

6-Methoxythiocarbonylmercapto-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **304**);

6-Mercapto-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **305**);

6-(1,1-Dimethyl-2-propynyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **306**);

6-*tert*-Butylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **307**);

6-Bromo-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **308**);

6-Bromo-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **309**);

6- *tert*-Butylamino-2-isopropyloxy-4-trifluoromethylquinolines (Compound **310**);

6-(1-Piperdinyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **311**);

6-(1-Pyrrolidinyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **312**);

6-(1-Morpholino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **313**);

(±)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **314**);

(+)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **315**);

(-)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **316**);

6-(N-phenylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **317**);

6-(N-phenyl-N-ethylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **319**);

6-(N-phenyl-N-ethylamino)-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **320**);

6-(N-phenyl-N-2,2,2-trifluoroethylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **321**);

(±)-6-(3-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **322**);

6-(4-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **323**);

6-(*cis*-3,5-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **324**);

6-(2,6-*cis*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **325**);

6-(2,6-*trans*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **326**);

(±)-6-(2-Methyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **327**);

6-(2,5-*cis*-Dimethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **328**);

(±)-6-(2,5-*trans*-Dimethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **329**);

6-(1-Azepano)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **330**);

(±)-6-(2-Hydroxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)--quinolinone (Compound **331**);

6-(2,5-cis-Dimethyl-1-pyrrolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **332**);

(±)-6-(2-Propyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **333**);

(±)-6-(2-Methoxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **334**);

(±)-6-(2-Ethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **335**);

6-(1-Cycloheptylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **336**);

(±)-6-(2-Ethoxycarbonyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **337**);

(±)-6-(2-Isopropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **338**);

(±)-6-(2-Hydroxycarbonyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **339**);

6-(3,5-*cis*-Dimethyl-1-piperazino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **340**);

(±)-6-(2-Benzyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **341**);

(±)-6-(5-Methyl-2-oxo-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **342**);

(±)-6-(2-(2-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **343**);

(±)-6-(3-Hydroxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **344**);

(±)-6-(3-Acetyloxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **345**);

(±)-6-(3-Hydroxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **346**);

6-(1-Indolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **347**);

6-(1-Tetrahydroquinolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **348**);

6-(2-Tetrahydroisoquinolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **349**);

(±)-6-(1,3,3-Trimethyl-6-azabicyclo[3.2.1]octanyl-6-)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **350**)

(±)-6-(2-Trifluoromethyl-5-*cis*-methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **351**);

(±)-6-(2-Trifluoromethyl-5-*trans*-methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **352**);

6-N-(1-Hydroxyisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **353**);

(±)-6-(2-Trifluoromethyl-5-cis-ethyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **354**);

(±)-6-(2-Trifluoromethyl-5-trans-ethyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **355**);

(±)-6-(5-Methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **356**);

6-(2,5-Dimethyl-1-pyrrolyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **357**);

6-(N-2,2,2-Trifluoroethyl-N-3,3,3-trifluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **358**);

6-(N-3,3,3-Trifluoropropyl)amino-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **360**);

6-bis-N,N-Thiomethoxymethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **361**);

6-bis-N,N-Thiomethoxymethylamino-4-trifluoromethyl-2-thiomethoxymethyloxyquinoline (Compound **362**);

(±)-6-(2,5-*trans*-Diethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **363**);

6-(2,5-*cis*-Diethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **364**);

(±)-6-(2,5-*trans*-Dipropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **365**);

6-(2,5-*cis*-Dipropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **366**);

6-(2,5-Dipropyl-1-pyrrolo)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **367**);

6-(2,5-*cis*-Dibutyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **368**);

(±)-6-(2,5-*trans*-Dibutyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **369**);

6-(2,6-*cis*- Diethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **370**);

(±)-6-(2,6-*trans*-Diethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **371**);

6-(2,6-*cis*- Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **372**);

(±)-6-(2,6-*trans*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **373**);

6-(N-Propyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **374**);

6-Amino-4-methyl-2(1*H*)-quinolinone (Compound **375**);

6-(bis-2,2,2-Trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **377**);

6-(2,5-Dimethyl-1-pyrrolyl)-4-methyl-2(1*H*)-quinolinone (Compound **378**);

(±)-6-(2,5-*trans*-dimethyl-1-pyrrolidino)-4-methyl-2(1*H*)-quinolinone (Compound **379**);

6-(2,5-*cis*-dimethyl-1-pyrrolidino)-4-methyl-2(1*H*)-quinolinone (Compound **380**);

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **381**);

6-(N-2,2,2-Chlorodifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **382**);

6-(bis-N,N-2,2,2-Chlorodifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **383**);

6-(N-2,2,2-Chlorodifluoroethyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **384**);

6-N-Ethylamino-4-methyl-2(1*H*)-quinolinone (Compound **385**);

6-(N-Ethyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **386**);

6-N,N-Diethylamino-4-methyl-2(1*H*)-quinolinone (Compound **387**);

6-(bis-2,2,2-trifluoroethyl)amino-4-ethyl-2(1*H*)-quinolinone (Compound **388**);

6-Amino-4-ethyl-2(1*H*)-quinolinone (Compound **389**);

6-(bis-2,2,2-trifluoroethyl)amino-4-isopropyl-2(1*H*)-quinolinone (Compound **391**);

6-Amino-4-isopropyl-2(1*H*)-quinolinone (Compound **392**);

7-Fluoro-6-(bis-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **393**);

7-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **394**);

5-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **395**);

6-Amino-7-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **396**);

8-Fluoro-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **397**);

8-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 316); 6-Amino-8-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **399**);

8-Fluoro-6-(N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **400**);

8-Fluoro-6-(N-2,2,2-trifluoroethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **401**);

6-Amino-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **402**);

3-Fluoro-6-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **403**);

3-Fluoro-6-(bis-2,2,2-trifluorofluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **404**);

6-(bis-Isobutylamino)-4-methyl-2(1*H*)-quinolinone (Compound **405**);

3-Fluoro-6-(N-methyl-N-2,2,2-trifluorofluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **406**);

7-Bromo-6-isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **407**);

6-Amino-7-bromo-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **408**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-hydroxy-2(1*H*)-quinolinone (Compound **409**);

6-amino-4-hydroxy-2(1*H*)-quinolinone (Compound **410**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-methoxy-2(1*H*)-quinolinone (Compound **411**);

6-amino-4-methoxy-2(1*H*)-quinolinone (Compound **412**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-difluoromethyl-2(1*H*)-quinolinone (Compound **413**);

6-amino-4-difluoromethyl-2(1*H*)-quinolinone (Compound **414**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **415**);

6-amino-2(1*H*)-quinolinone (Compound **416**);

4-Chloro-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **417**);

6-amino-4-chloro-2(1*H*)-quinolinone (Compound **418**);

7-Methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **419**);

5,7-Dimethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **420**);

(*R*)-6-(2-Hydroxymethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **421**);

(*R*)-6-(2-Methoxycarbonyl-1-pyrrolidino)-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **422**);

(*R*)-6-(2-Methoxymethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **423**);

(±)-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **424**);

(±)-6-(2-Cyanothiomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **425**);

(±)-6-(2-Thiomethoxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **426**);

(±)-6-(2-Cyanomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **427**);

(±)-6-(2-Bromomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **428**);

(±)-6-(2-Iodomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **429**);

(+)*R*-6-(2-Iodomethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **430**);

(±)-6-(2-Fluoromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **431**);

(+)S-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **432**);

(-)R-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **433**);

(+)*R*-6-(2-Chloromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **434**);

(-)*S*-6-(2-Chloromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **435**);

R-6-(2-Difluoromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **436**);

(±)-6-(2*l*-(1*l*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **437**);

(±)-6-(2*l*-(1*u*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **438**);

(±)-6-(2-Formyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **439**);

(±)-6-(2-Difluoromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **440**);

(±)-6-(2-Aminomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **441**);

(*R*)-6-(2-Vinyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **442**);

(*R*)-6-(2-Formyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **443**);

(±)-6-(2-Vinyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **444**);

(±)-6-(2-Benzyloxyethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **445**);

(±)-6-(2-(2,2-Difluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **446**);

(±)-6-(2-Trifluoroacetamidomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **447**);

(±)-6-(2-(2-Ethoxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **448**);

(±)-6-(2-(4-Trifluoromethyl)benzyloxyethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **449**);

(+)-6-(2*R*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **450**);

(-)6-(2*R*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **451**);

6-(2*S*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **452**);

6-(2*S*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **453**);

(±)-6-(2*l*-(1*l*-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **454**);

(±)-6-(2*l*-(1*u*-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **455**);

(-)-6-(2*S*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **456**);

(+)-6-(2*R*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **457**);

(+)-6-(2*R*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **458**);

(-)-6-(2*S*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 459);

(±)-6-(2*l*-(1*l*-Acetyloxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 460);

(±)-6-(2*l*-(1*u*-Acetyloxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 461);

(±)-6-(2*l*-(1*u*-Methoxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 462);

(±)-6-(2*l*-(1*l*-Methoxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 463);

7-Methoxy-6-(N-methyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 464);

4-Amino-2-methoxy-N-2,2,2-trifluoroethylaniline (Compound 466);

7-Methoxy-6-(N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 467);

7-Methoxy-6-(N-ethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 468);

7-Hydroxy-6-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 469);

6-(N-Cyclopropylmethyl-N-2,2,2-trifluoroethyl)amino-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 470);

6-(N-Cyclopropylmethyl-N-2,2,2-trifluoroethyl)amino-7-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 471);

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 472);

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-7-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 473);

6-(bis-2,2,2-Trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound 474);

6-Amino-4-trifluoromethylcoumarin (Compound 475);

(±)-3,4-Dihydro-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound 476);

6-(2,2,2-trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound 477);

6-(N-Isopropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound 478);

6-N-Isobutylamino-4-trifluoromethylcoumarin (Compound 479);

6-N,N-Diethylamino-4-trifluoromethylcoumarin (Compound 480);

6-N,N-Dipropylamino-4-trifluoromethylcoumarin (Compound 481);

6-N-Propylamino-4-trifluoromethylcoumarin (Compound 482);

6-(N-Isobutyl-N-propylamino)-4-trifluoromethylcoumarin (Compound 483);

6-(N-2,2,2-Trifluoroethyl-N-propylamino)-4-trifluoromethylcoumarin (Compound 484);

1,4-Dihydro-4,4-dimethyl-6-methylamino-1,3-benzo[d]oxazin-2-one (Compound 485);

6-Amino-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound 487);

1,4-Dihydro-4,4-dimethyl-6-dimethylamino-1,3-benzo[d]oxazin-2-one (Compound 488);

1,4-Dihydro-4,4-dimethyl-6-dipropylamino-1,3-benzo[d]oxazin-2-one (Compound 489);

1,4-Dihydro-4,4-dimethyl-6-(bis-N,N-2,2,2-trifluoroethyl)amino-1,3-benzo[d]oxazin-2-one (Compound 490);

1,4-Dihydro-4,4-dimethyl-6-(N-2,2,2-trifluoroethyl)amino-1,3-benzo[d]oxazin-2-one (Compound 491);

(±)-1,4-Dihydro-4-methyl-6-diallylamino-1,3-benzo[d]oxazin-2-one (Compound 492);

(±)-6-Amino-1,4-dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound 494);

6-Amino-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound 495);

6-Diallylamino-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound 497);

3,4-Dihydro-4,4-dimethyl-6-dipropylamino-2(1*H*)-quinolinone (Compound 498);

3,4-Dihydro-4,4-dimethyl-6-propylamino-2(1*H*)-quinolinone (Compound 499);

3,4-Dihydro-4,4-dimethyl-6-(N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound 500);

3,4-Dihydro-4,4-dimethyl-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound 501);

3,4-Dihydro-6-(N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound 502);

6-Amino-3,4-dihydro-2(1*H*)-quinolinone (Compound **503**);

3,4-Dihydro-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **505**);

5-(bis-N,N-2,2,2-Trifluoroethyl)amino-3,3-spirocyclohexyl-2-indolone (Compound **506**);

5-Amino-3-spirocyclohexyloxindole (Compound **507**);

7-(bis-N,N-2,2,2-Trifluoroethyl)amino-1,4-benzoxazin-3(4*H*)-one (Compound **508**);

7-amino-1,4-benzoxazin-3(4*H*)-one (Compound **509**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-2,4-dichloroquinoline (Compound **510**);

6-amino-1,4-dichloro-2(1H)-quinolinone (Compound **511**);

7-Amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **512**);

7-Propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **513**);

7-Isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **514**);

7-(2,2-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **515**);

7-(2-Methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **516**);

7-Methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **517**);

7-Dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **518**);

7-Benzylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **519**);

7-(2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **520**);

7-Butylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **521**);

7-Ethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **522**);

7-(N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **523**);

7-Cyclohexylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **524**);

7-Cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **525**);

7-Cyclobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **526**);

7-(2-Hydroxy-2-methylpropionyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **527**);

7-(Trifluoroacetamido)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **528**); 1-Methyl-7-methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **529**);

1-Methyl-7-dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **530**);

1-Methyl-7-(N-methyl-N-isopropylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **531**);

1-Methyl-7-(2,2,2-trifluoromethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **532**);

3-Fluoro-7-(2,2,2-trifluoromethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **533**);

3-Fluoro-7-amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **534**);

3-Fluoro-7-isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **535**);

3-Fluoro-7-cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **536**);

3-Fluoro-7-cyclohexylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **537**);

3-Fluoro-7-cyclobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **538**);

3-Fluoro-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **539**);

3-Fluoro-1-methyl-7-(N-methyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **540**);

3-Fluoro-1-methyl-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **541**);

6-Fluoro-7-amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **542**);

6-Fluoro-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **543**);

6-Fluoro-7-isobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **544**);

6-Fluoro-1-methyl-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **545**);

6-Fluoro-1-methyl-7-(N-methyl-N-propylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **546**);

7-Amino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **547**);

7-Isobutylamino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **548**);

7-Propylamino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **549**);

7-(1,1-Dimethyl-3-oxobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **550**);

7-(1,1,3-Trimethyl-3-hydroxybutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **551**);

7-(1,1,3-Trimethyl-3-butenylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **552**);

7-(1-Phenylaminocarbonylisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **553**);

7-(2-Hydroxy-1,1-dimethylethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **556**);

7-(N-1-Formylisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **558**);

7-(1,1-Dimethylallyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **559**);

7-(1,1-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **560**);

7-(1-Methyl-1-acetylenylpropyl)amino]-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **561**);

7-(1-Ethyl-1-methylpropyl)amino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **562**);

8-Methyl-7-(3-methyl-2-butenyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **563**);

8-Methyl-7-(3-methylbutyl)amino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **566**);

8-Methyl-7-propylamino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **567**);

8-Methyl-7-isobutylamino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **569**);

7-Amino-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **571**);

7-Isobutylmino-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **574**);

7-(2-Picolylamino)-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **575**);

7-Amino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **576**);

7-Amino-6-ethyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **577**);

7-Amino-6-propyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **580**);

7-Amino-6-*sec*-butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **581**);

7-Amino-6-cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **582**);

6-Ethyl-7-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **585**);

6-Ethyl-7-methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **586**);

6-Ethyl-7-dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **587**);

6-Isobutyl-7-methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **588**);

7-(1-Morpholino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **589**);

5-Amino-7-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **592**);

5-Propylamino-7-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **594**);

7-Chloro-5-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **595**);

5-Amino-6-bromo-3,4-dihydro-4-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **596**);

6-Bromo-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **598**);

6-(bis-N,N-2,2,2-trifluoroethyl)amino-5-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **600**);

6-amino-5-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **601**);

6-(N-2,2,2-Trifluoroethyl)amino-5-propyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **602**);

6-amino-5-propyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **603**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-propyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **604**);

6-(N-2,2,2-Trifluoroethyl)amino-5-ethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **605**);

6-amino-5-ethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **606**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-ethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **607**);

6-(N-2,2,2-Trifluoroethyl)amino-5-(3,3,3-trifluoropropyloxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **608**);

6-amino-5-(3,3,3-trifluoropropyloxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **609**);

6-(N-2,2,2-Trifluoroethyl)amino-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **610**);

6-amino-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **611**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **612**);

6-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **613**);

6-Chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **614**);

6-Isopropyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **615**);

6-Cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **616**);

6-(1- *trans*-Propenyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **617**);

6-Cyclohexyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **618**);

7-Fluoro-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **619**);

5,7-Difluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **620**);

6-Methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **621**);

6-Hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **622**);

6-Benzyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **623**);

6-(3-Pentyloxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **624**);

6-(1-Hydroxy-3,3,5,5-tetramethyl)cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **625**);

6-(3,3,5,5-Tetramethyl)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **626**);

6-(5,5-Dimethycyclopentenyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **627**);

6-(2,2-Dimethycyclopentyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **628**);

6-(1-Hydroxycyclohexyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **629**);

6-Cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **630**);

6-Cyclohexyl-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **631**);

6-Cyclopentenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **632**);

6-Cycloheptenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **633**);

6-Bromo-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **634**);

6-Cyclohexenyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **635**);

6-Cyclohexyl-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **636**);

6-Bromo-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **637**);

6-Cyclopentyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **638**);

(Z)-6-(1-Propyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **639**);

(E)-6-(1-Propyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **640**);

6-(1-Propyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **641**);

(E)-6-(1-Methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **642**);

(Z)-6-(1-Methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **643**);

(±)-6-(1-Methyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **644**);

(E)-6-(1-Ethyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **645**);

(Z)-6-(1-Ethyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **646**);

6-(1-Ethyl)propyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **647**);

6-(1-Isopropyl-2-methyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **648**);

6-(1-Isopropyl-2-methyl)propyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **649**);

(Z)-6-(1-Isobutyl-3-methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **650**);

(E)-6-(1-Isobutyl-3-methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **651**);

6-(1-Isobutyl-3-methyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **652**);

6-(1-Propyl)butyl-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **653**);

6-(3-Oxo-1-)cyclopentenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **654**);

6-(3-Oxo-1-)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **655**);

6-(3-Oxo-1-)cyclopentenyl-3-methyl-4-difluoromethyl-2(1*H*)-quinolinone (Compound **656**);

6-(3-Oxo-1-)cyclohexenyl-3-methyl-4-difluoromethyl-2(1*H*)-quinolinone (Compound **657**);

(±)-6-(3-Hydroxy-1-)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **658**);

6-(1-Hydroxy-1,1-diphenyl)methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **659**);

6-Diphenylmethyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **660**);

6-(3-hydroxy-3-methyl-1-)butynyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **661**);

6-(1-Hydroxy)cyclopentyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **662**);

6-Bromo-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **663**);

6-(1-Cyclopentenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **664**);

6-Cyclopentyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **665**);

6-(1-Hydroxy)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **666**);

6-(1-Cyclohexenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **667**);

6-Cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **668**);

6-(1-Hydroxy)cycloheptyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **669**);

6-(1-Cycloheptenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **670**);

6-(1-Cycloheptyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **671**);

6-(2,6,6-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **672**);

(±)-6-(3,3,5-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **673**);

(±)-6-(3,5,5-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **674**);

(±)-6-(5-Methyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **675**);

(±)-6-(3-Methyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **676**);

(±)-6-(2,6-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **677**);

(±)-6-(2-Bicyclo[2.2.1]heptenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **678**);

(±)-6-(4,5-*trans*-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **679**);

(±)-6-(3,4-*trans*-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **680**);

6-(6,6-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **681**);

6-(5,5-Dimethyl-1-)cyclopentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **682**);

(±)-6-(3,3,5-*cis*-Trimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **683**);

(±)-6-(3,3,5-*trans*-Trimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **684**);

(±)-6-(3-*cis*-Methyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **685**);

(±)-6-(3-*trans*-Methyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **686**);

(±)-6-(2,6-cis,cis-Dimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **687**);

(*E*)-6-(1,4-Dimethyl-1-)pentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **688**);

6-(1-Cyclohexenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **689**);

6-(3-Oxo-1-)cyclopentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **690**);

6-(3-Oxo-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **691**);

(±)-6-(3-Hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **692**);

(±)-6-(3-*cis*-Hydroxy)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **693**);

(±)-6-(3-Butyl-3-hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **694**);

6-(3-Oxo-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **695**);

6-Bromo-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **696**);

(±)-6-(3-Hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **697**);

(±)-6-(1-Cyclohexenyl)-1,4-dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **698**);

(±)-6-Bromo-1,4-dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **700**);

6-(1-Cyclohexenyl)-1,4-dihydro-4,4,5-trimethyl-1,3-benzo[d]oxazin-2-one (Compound **701**);

6-Bromo-1,4-dihydro-4,4,5-trimethyl-1,3-benzo[d]oxazin-2-one (Compound **704**);

6-(1-Cyclohexenyl)-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **705**);

6-Bromo-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **706**);

6-Cyclohexyl-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **707**);

(±)-8-Bromo-6-(1-cyclohexenyl)-1,4-dihydro-4-trifluoromethyl-1,3-benzo[d]oxazin-2-one (Compound **708**);

(±)-6,8-Dibromo-1,4-dihydro-4-trifluoromethyl-1,3-benzo[d]oxazin-2-one (Compound **711**);

5-(3-Oxo-1-)cyclohexenyl-3,3-dimethyl-2-indolone (Compound **712**);

5-Bromo-3,3-dimethyl-2-indolone (Compound 542); (±)-5-(3-Hydroxy-1-)cyclohexenyl-3,3-dimethyl-2-indolone (Compound **714**);

(±)-5-(3-Oxocyclohexyl)-3,3-dimethyl-2-indolone (Compound **715**);

(±)-5-(3-Oxocyclohexyl)-3,3-dimethyl-2-indolone (Compound 544); 5-Cyclohexyl-3,3-spirocyclohexyl-2-indolone (Compound **716**);

5-Bromo-3,3-spirocyclohexyl-2-indolone (Compound **717**);

5-Cyclopentyl-3,3-spirocyclohexyl-2-indolone (Compound **718**);

6-(1-Hydroxycyclohexyl)-2(3*H*)-benzothiozolone (Compound **719**);

6-Cyclohexenyl-2(3*H*)-benzothiozolone (Compound **720**);

3,4-Dihydro-6-isopropyl-3-methyl-2(1*H*)-quinazolinone (Compound **721**);

6-Bromo-3,4-dihydro-3-methyl-2(1*H*)-quinazolinone (Compound **722**);

1-Benzyl-6-bromo-3,4-dihydro-3-methyl-2(1*H*)-quinazolinone (Compound **723**);

1-Benzyl-6-cyclohexyl-3,4-dihydro-3-methyl-2(1*H*)-quinazolinone (Compound **724**);

6-(2,3-Difluoro)phenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **725**);

4-Trifluoromethyl-6-(3-nitro)phenyl-2(1*H*)-quinolinone (Compound **727**);

4-Trifluoromethyl-6-(3,5-dichloro)phenyl-2(1*H*)-quinolinone (Compound **728**);

4-Trifluoromethyl-6-(3-fluoro-5-N-hydroxyliminomethyl)phenyl-2(1*H*)-quinolinone (Compound **729**);

4-Trifluoromethyl-6-(3-fluoro-5-formylmethylphenyl)-2(1*H*)-quinolinone (Compound **730**);

4-Trifluoromethyl-6-(3-fluoro-5-cyano)phenyl-2(1*H*)-quinolinone (Compound **731**);

4-Trifluoromethyl-6-(3-fluoro-5-chloro)phenyl-2(1*H*)-quinolinone (Compound **732**);

4-Trifluoromethyl-6-(4-hydroxymethyl)phenyl-2(1*H*)-quinolinone (Compound **734**);

4-Trifluoromethyl-6-(3-acetylphenyl)-2(1*H*)-quinolinone (Compound **735**);

4-Trifluoromethyl-6-(4-ethylphenyl)-2(1*H*)-quinolinone (Compound **736**);

4-Trifluoromethyl-6-(3-ethoxylphenyl)-2(1*H*)-quinolinone (Compound **737**);

4-Trifluoromethyl-6-(3-methylphenyl)-2(1*H*)-quinolinone (Compound **738**);

4-Trifluoromethyl-6-(3-trifluoromethylphenyl)-2(1*H*)-quinolinone (Compound **739**);

4-Trifluoromethyl-6-(3-chlorophenyl)-2(1*H*)-quinolinone (Compound **740**);

4-Trifluoromethyl-6-(3-fluorophenyl)-2(1*H*)-quinolinone (Compound **741**); 4-Trifluoromethyl-6-(2-methylphenyl)-2(1*H*)-quinolinone (Compound **742**);

4-Trifluoromethyl-6-(4-formyl)phenyl-2(1*H*)-quinolinone (Compound **743**);

4-Trifluoromethyl-6-(4-*tert*-butylphenyl)-2(1*H*)-quinolinone (Compound **744**);

4-Trifluoromethyl-6-(2-methoxyphenyl)-2(1*H*)-quinolinone (Compound **745**);

4-Trifluoromethyl-6-(2-fluorophenyl)-2(1*H*)-quinolinone (Compound **746**);

4-Trifluoromethyl-6-(4-acetylphenyl)-2(1*H*)-quinolinone (Compound **747**);

4-Trifluoromethyl-6-(4-methylphenyl)-2(1*H*)-quinolinone (Compound **748**);

4-Trifluoromethyl-6-(4-fluorophenyl)-2(1*H*)-quinolinone (Compound **749**);

4-Trifluoromethyl-6-(4-methoxyphenyl)-2(1*H*)-quinolinone (Compound **750**);

4-Trifluoromethyl-6-(3,5-bis-trifluoromethyl)phenyl-2(1*H*)-quinolinone (Compound **751**);

4-Trifluoromethyl-6-(4-trifluoromethoxyphenyl)-2(1*H*)-quinolinone (Compound **752**);

4-Trifluoromethyl-6-(2,4-dichlorophenyl)-2(1*H*)-quinolinone (Compound **753**);

3-Fluoro-4-trifluoromethyl-6-(2-fluorophenyl)-2(1*H*)-quinolinone (Compound **754**);

3-Fluoro-4-trifluoromethyl-6-(2,4-dichlorophenyl)-2(1*H*)-quinolinone (Compound **755**);

4-Trifluoromethyl-6-(4-hydroxyphenyl)-2(1*H*)-quinolinone (Compound **756**);

6-Bromo-4-methyl-2(1*H*)-quinolinone (Compound **757**);

4-Methyl-6-(3-methoxyphenyl)-2(1*H*)-quinolinone (Compound **758**);

4-Methyl-6-(3-chlorophenyl)-2(1*H*)-quinolinone (Compound **759**);

4-Methyl-6-(3-chloro-2-methylphenyl)-2(1*H*)-quinolinone (Compound **760**);

4-Methyl-6-(2,3-dichlorophenyl)-2(1*H*)-quinolinone (Compound **761**);

4-Methyl-6-(2,4-dichlorophenyl)-2(1*H*)-quinolinone (Compound **762**);

4-Methyl-6-(2-methylphenyl)-2(1*H*)-quinolinone (Compound **763**);

4-Trifluoromethyl-6-phenyl-2(1*H*)-quinolinone (Compound **764**);

4-Trifluoromethyl-6-propio-2(1*H*)-quinolinone (Compound **765**);

4-Trifluoromethyl-6-(1-ethylaminopropyl)-2(1*H*)-quinolinone (Compound **767**);

4-Trifluoromethyl-6-(1-N-ethyl-N-methylaminopropyl)-2(1*H*)-quinolinone (Compound **768**);

4-Trifluoromethyl-6-(1-hydroxy-1-methyl-2-oxopropyl)-2(1*H*)-quinolinone (Compound **769**);

4-Trifluoromethyl-6-(4,4,4-trifluoro-1(*E*)-butenyl)-2(1*H*)-quinolinone (Compound **771**);

4-Trifluoromethyl-6-(4,4,4-trifluorobutyro)-2-isopropyloxyquinoline (Compound **772**);

4-Trifluoromethyl-6-(1-hydroxy-4,4,4-trifluorobutyl)-2-isopropyloxyquinoline (Compound **773**);

4-Trifluoromethyl-6-(1-(3,3,3-trifluoropropyl)-1(*E*)-propenyl)-2(1*H*)-quinolinone (Compound **774**);

4-Trifluoromethyl-6-(1-ethyl-1-hydroxy-4,4,4-trifluorobutyl)-2-isopropyloxyquinoline (Compound **775**);

4-Trifluoromethyl-6-(1-ethyl-4,4,4-trifluoro-1(*E*)-butenyl)-2(1*H*)-quinolinone (Compound **776**);

4-Trifluoromethyl-6-(1-ethyl-4,4,4-trifluoro-1(*Z*)-butenyl)-2(1*H*)-quinolinone (Compound **777**);

2-Chloro-4-trifluoromethyl-6-(bis-N,N-2,2,2-trifluoroethyl)aminoquinoline (Compound **778**);

2-Methoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **779**);

2-Isopropyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **780**);

2-Ethoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **781**);

2-Acetyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **782**);

2-(2-Dimethylamino)ethoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **783**);

2-Isobutyryloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **784**);

2-(2,2-Dimethyl)propyryloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)-aminoquinoline (Compound **785**);

2-N,N-Dimethylcarbamyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)-aminoquinoline (Compound **786**);

2-Cyano-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **787**);

4-Trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone oxime (Compound **788**);

Representative PR modulator compounds (i.e., agonists and antagonists) according to the present invention include:

6-(N-Ethyl-N-2,2-dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **242**);

(±)-6-(N-Propyl-N-1-methylbutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **251**);

6-Cyclohexyl-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **631**);

6-(1-Cyclohexenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **667**);

6-(1-Cycloheptyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **671**);

6-(1-Cyclohexenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **689**);

6-(3-Oxo-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **695**);

(±)-6-(3-Hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **697**);

6-(2,3-Difluoro)phenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **725**);

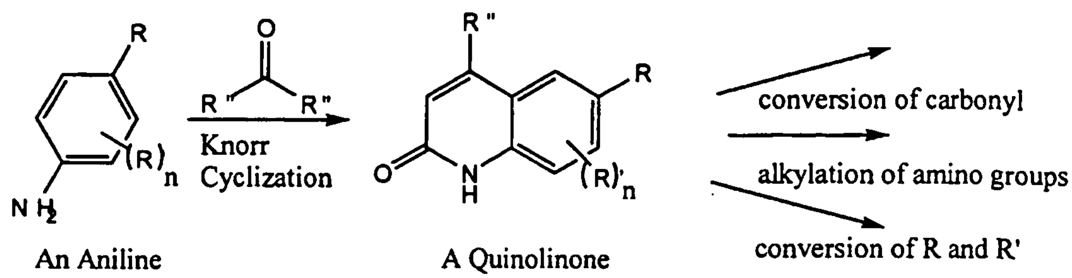
4-Trifluoromethyl-6-(3-nitro)phenyl-2(1*H*)-quinolinone (Compound **727**);

4-Trifluoromethyl-6-(3-fluoro-5-cyano)phenyl-2(1*H*)-quinolinone (Compound **731**);

4-Trifluoromethyl-6-(3-acetylphenyl)-2(1*H*)-quinolinone (Compound **735**).

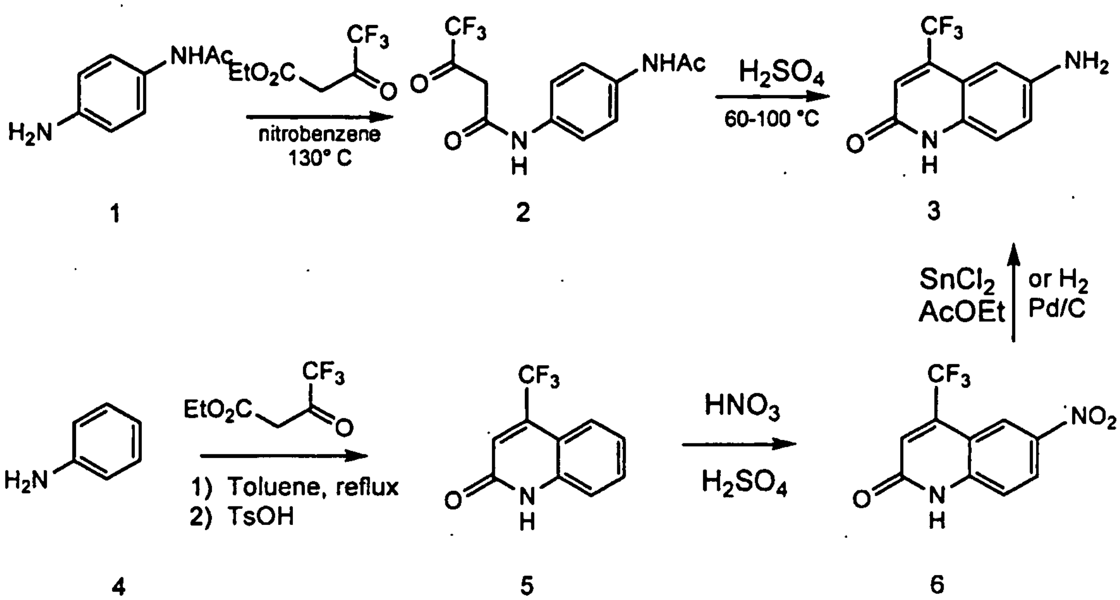
The sequences of steps for several general schemes to synthesize the compounds of the present invention are shown below. In each of the Schemes the R groups (e.g., R^1, R^2, etc.) correspond to the specific substitution patterns noted in the Examples. However, it will be understood by those skilled in the art that other functionalities disclosed herein at the indicated positions of compounds of formulas I through XXXIII also comprise potential substituents for the analogous positions on the structures within the Schemes.

Preparation of Quinolinone Compounds from Anilines



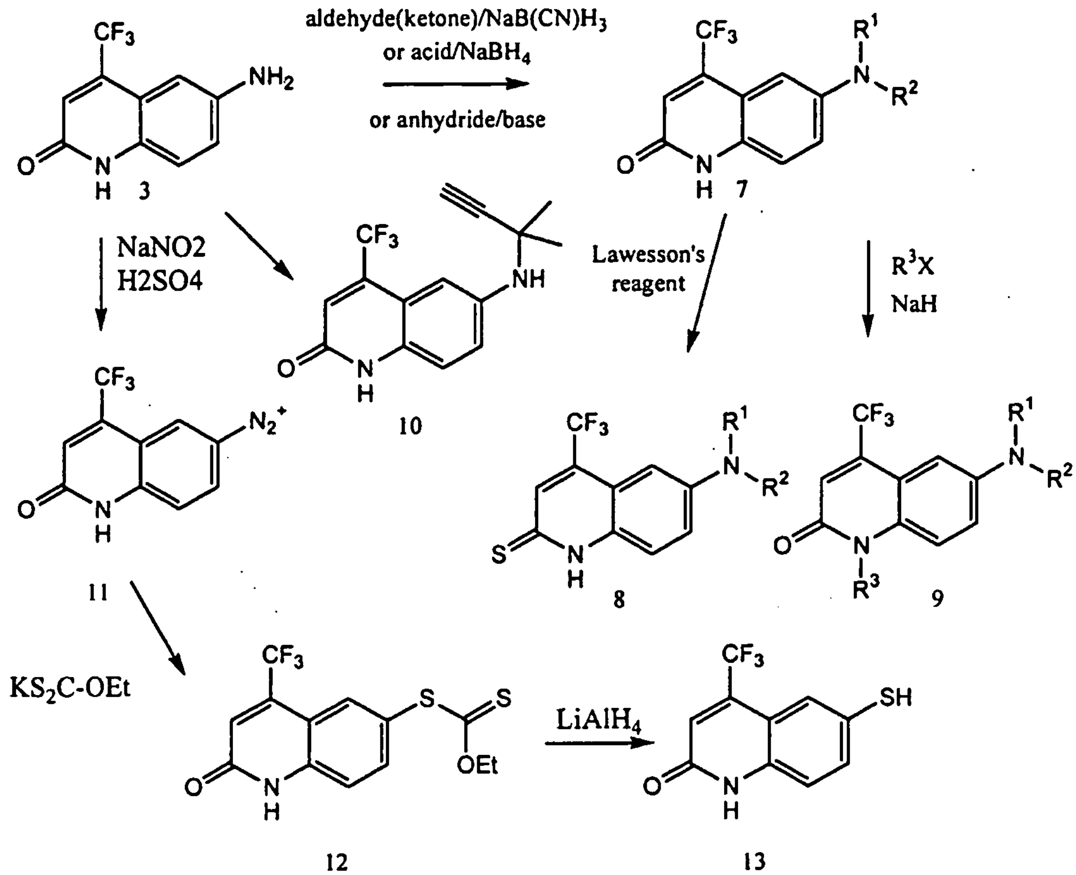
The above reaction sequence shows the general formulation of quinolinone compounds which are modulators of androgen and progesterone receptors. In the above reaction sequence, an aniline compound is converted to a quinolinone compound by a Knorr cyclization with an alpha-keto ester compound. The quinolinone may then be converted to various derivatives including but not limited to thioquinolinones, quinolines, alkylated quinolinones, and functionalized quinolinones. In the above scheme, R represents various aromatic substituents contained on the aniline compound known to those skilled in the art. The R group on the quinolinone compounds may be interconverted to various substituents including but not limited to nitro, amino, alkylamino, halogen, alkyl, aryl, dialkylamino, pyrrole, and oxazolidene groups by various chemical reactions known to those skilled in the art. The R' group represents various aromatic subsitutents known to those skilled in the art and may originate from any of the 3, 5, and 6 positions on the ring, and n may be from 0 to 3. The R' groups on the quinolinone compounds may also be interconverted to various substitutents by chemistry known to those skilled in the art to form derivative quinolinone compounds. Schemes I through VI below show various preferred embodiments of the current invention.

Scheme I



Scheme I describes a method to prepare quinolinone compounds such as Structure **5**, nitro-quinolinone compounds such as Structure **6**, and amino-2-quinolinone compounds such as Structure **3** through modified Knorr reactions. Thermal condensation of a 4-aminoacetanilide (Structure **1**) with a 3-ketoester, for example, ethyl 4,4,4-trifluoroacetoacetate in nitrobenzene affords a bis-amide such as Structure **2**. When a bis-amide compound of Structure **2** is treated with concentrated sulfuric acid at 60-100 °C, aminoquinolinone compounds of Structure **3** are produced. An alternate process of preparing 6-aminoquinolinone compounds such as Structure **3** starts with a similar Knorr reaction. The synthesis begins with reaction of an aniline such as Structure **4** and a 3-ketoester in refluxing toluene followed by treatment of a Lewis acid such as p-toluenesulfonic acid to produce a 2-quinolinone such as Structure **5**. Classic nitration of the 2-quinolinone (e.g., Structure **5**) selectively provides a 6-nitroquinolinone compound (e.g., Structure **6**). Reduction of the nitroquinolinone such as Structure 6 under standard reduction conditions (e.g., metal catalyzed hydrogenation or tin chloride reduction) affords aminoquinolinone compounds such as Structure **3**.

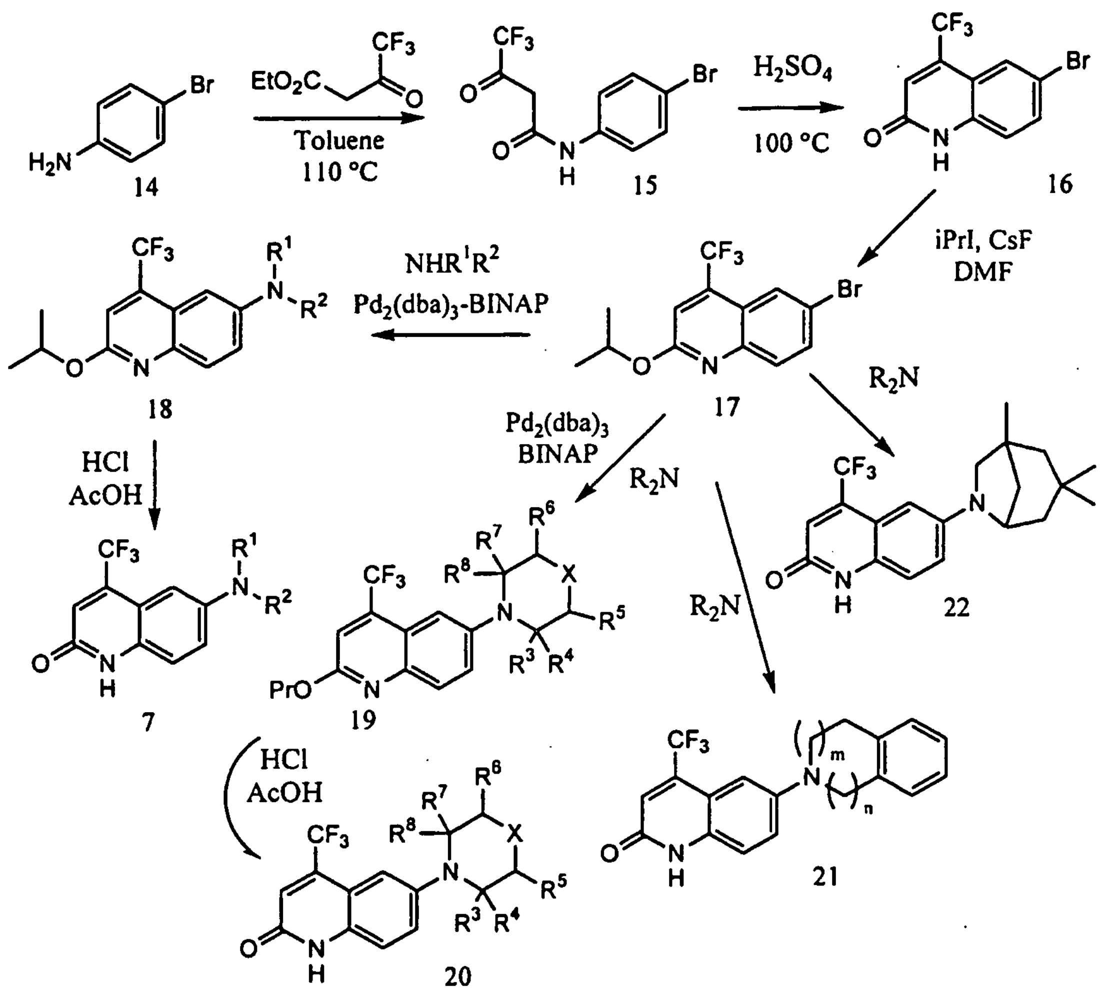
Scheme II



Scheme II describes the N-substitution of the 6-amino-2-quinolinone such as Structure **3** and the conversion of Structure **3** to mercapto analogues. A two-step sequential reductive alkylation of the aminoquinolinone (e.g., Structure **3**) with an aldehyde or ketone or acid in the presence of a reducing agent, such as sodium cyanoborohydride or sodium borohydride affords compounds of Structure **7**. Treatment of an amino-2-quinolinone compound (e.g., Structure **3**) with an acylating agent, such as acetyl chloride or anhydride, in the presence of a base such as pyridine or triethylamine provides amides or sulfonamides compounds as shown in Structure **7**. Treatment of quinolinones of Structure **7** with Lawesson's reagent provides a corresponding thioquinolinone compound of Structure **8**. Treatment of compounds of Structure 7 with an alkylating agent such as alkyl iodide in the presence of sodium hydride in a polar solvent, such as tetrahydrofuran gives compounds of Structure **9**. Direct alkylation of Structure **3** provides

compounds of Structure **10**. The mercapto analogues of Structures **12** and **13** are prepared through diazo intermediate of Structure **11**.

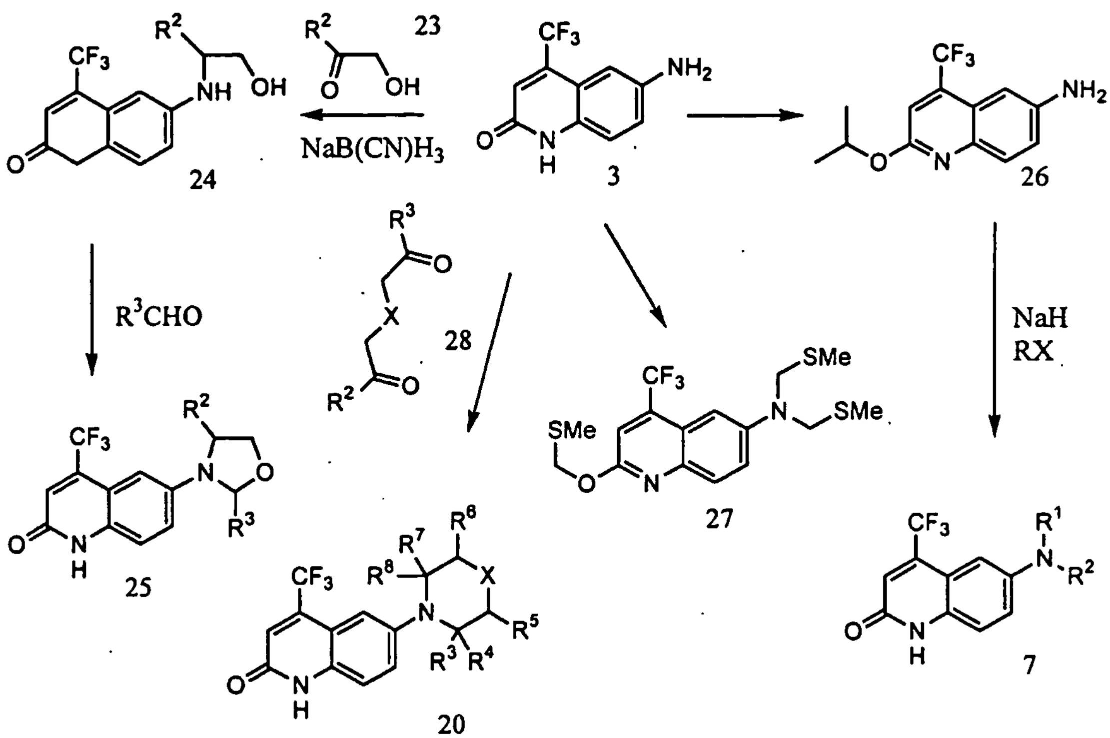
Scheme III



Scheme III describes an alternate method for the syntheses of 6-amino compounds of Structures **7**, **20**, **21** and **22**. The process begins with a step-wise Knorr reaction, in which 4-Bromoaniline (Structure **14**) and a 3-ketoester such as the trifluoroacetoacetate are heated in reflux in toluene provides an amide such as Structure **15** and heating in concentrated sulfuric acid affords 4-bromoquinolinone such as Structure **16**. Treatment of quinolinones such as Structure **16** with 2-iodopropane, catalyzed by cesium fluoride in DMF afford alkoxyquinoline compounds such as Structure **17**. Palladium-catalyzed coupling reaction between

bromoquinolines such as Structure **17** and alkylamines gives compounds of Structures **18** and **19**. Hydrolysis of the quinoline compounds (Structures **18** and **19**) in acidic condition provide compounds of Structures **7** and **20**. Compounds of Structures **21** and **22** are prepared in a similar fashion.

<u>Scheme IV</u>

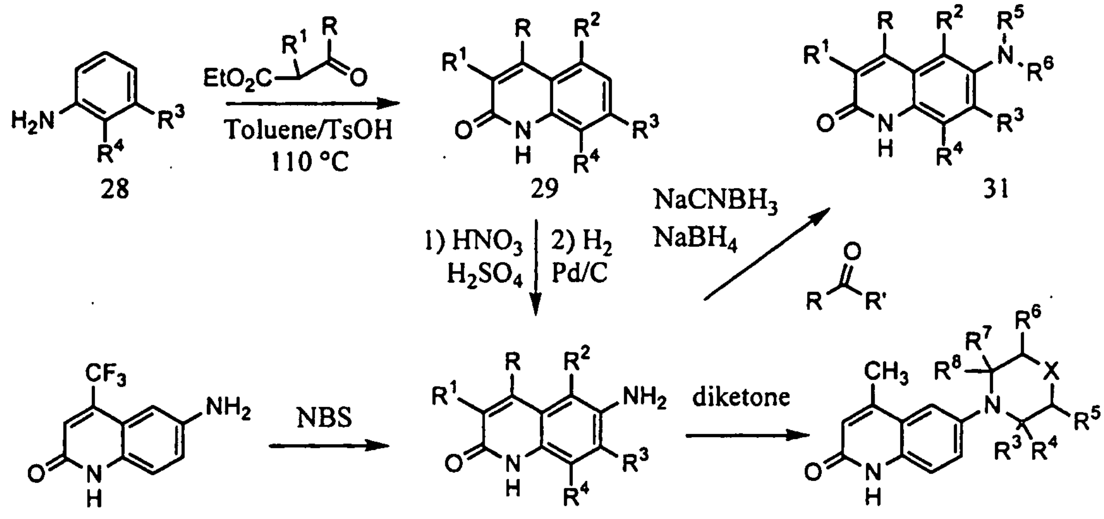


Scheme IV shows additional alkylation strategies of 6-aminoquinolinone of Structure 3 to provide 6-oxazolidine-quinolinone compounds (e.g., Structure 25), 6-cycloalkylamino-quinolinone compounds (e.g., Structure 20) and compounds of Structures 7 and 27.

The process of Scheme IV begins with reductive alkylation of an aminoquinolinone (e.g., Structure 3), with α-hydroxyketones of Structure 23 in the presence of a reducing agent such as sodium cyanoborohydride to provide compounds of Structure 24. Formation of an oxazolidine compound such as Structure 25 is carried out by treatment of an aminol compound such as Structure 24 with an aldehyde or its corresponding hydrate in the presence of an acid. Quinolinone compounds of Structure 20 are prepared by condensation of an aminoquinolinone (e.g., Structure 3) and a diketone such as Structure 28 in the presence of a reducing agent.

Compounds such as Structure 7 are prepared by alkylation of quinoline intermediate of Structure 26 derived from Structure 3 with an alkyl halide. Direct alkylation of Structure 3 with halides affords mixture compounds of Structures 7 and 27.

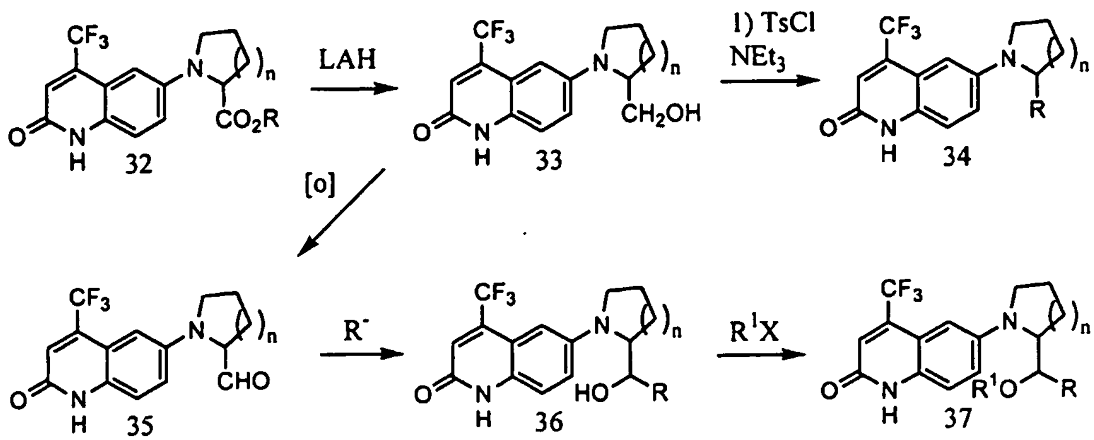
Scheme V



3 30 20a

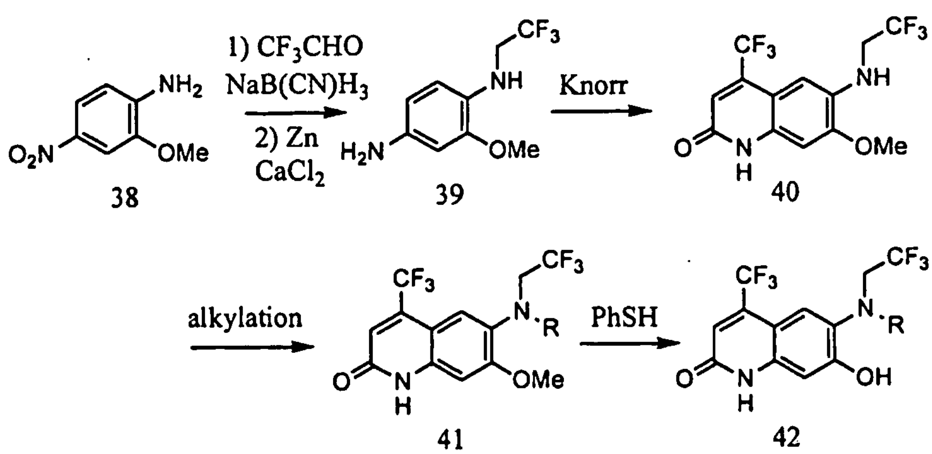
Scheme V shows the preparation of substituted quinolinones of Structures **20a** and **31** from anilines of Structure **28** or 6-aminoquinolinones such as Structure **3**. The process begins with a Knorr cyclization of a meta- or ortho-substituted aniline (e.g., Structure **28**) with a 3-ketoester to afford compounds of Structure **29**. Nitration of compounds such as Structure **29** followed by reduction of the nitro group affords predominantly 6-amino compounds of Structure **30**. Alternately compounds of Structure **30** are also obtained by modification of 6-aminoquinolinones such as Structure **3**. For example, bromination of compounds of Structure **3** with NBS provides a 7-bromo-2-quinolinone compound (e.g., Structure **30**, where R^3 = bromo). Quinolinone compounds as shown in Structures **20a** and **31** are synthesized in a similar fashion as that described in Schemes II and IV from the substituted 6-amino-2-quinolinones of Structure **30**.

Scheme VI



Scheme VI describes the side-chain modification of the 6-cycloamino-2-quinolinones of Structure **32**. The process of Scheme VI starts with the reduction of an ester derivative of Structure **32** to give hydroxycompounds of Structure **33**. Conversion of compounds of Structure **33** to tosylated analogues followed by nucleophilic substitution affords compounds of Structure **34**. Oxidation of compounds of Structure **33** provides the formyl derivatives of Structure **35**. Addition of a nucleophile to compounds of Structure **35** gives secondary alcohol analogues of Structure **36**. Further manipulation affords compounds of Structure **37**.

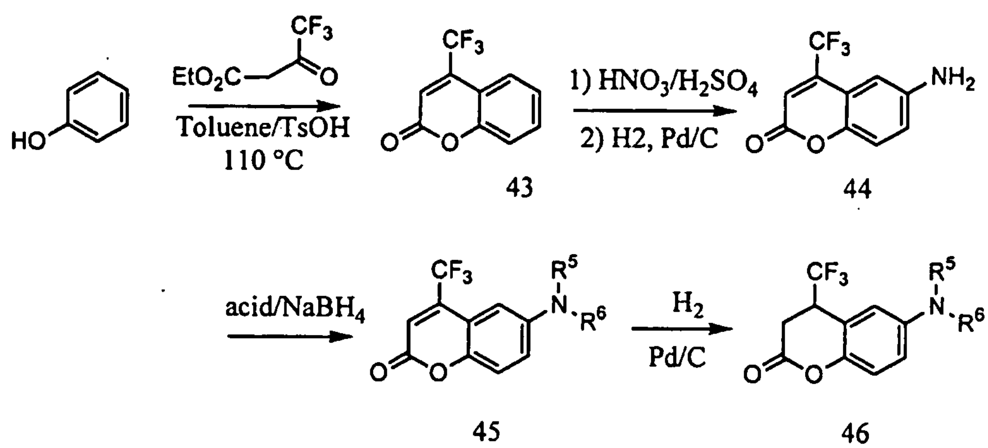
Scheme VII



Scheme VII describes Knorr reactions of substituted anilines to produce functionalized quinolinone compounds. The process of Scheme VII starts with alkylation of an aniline

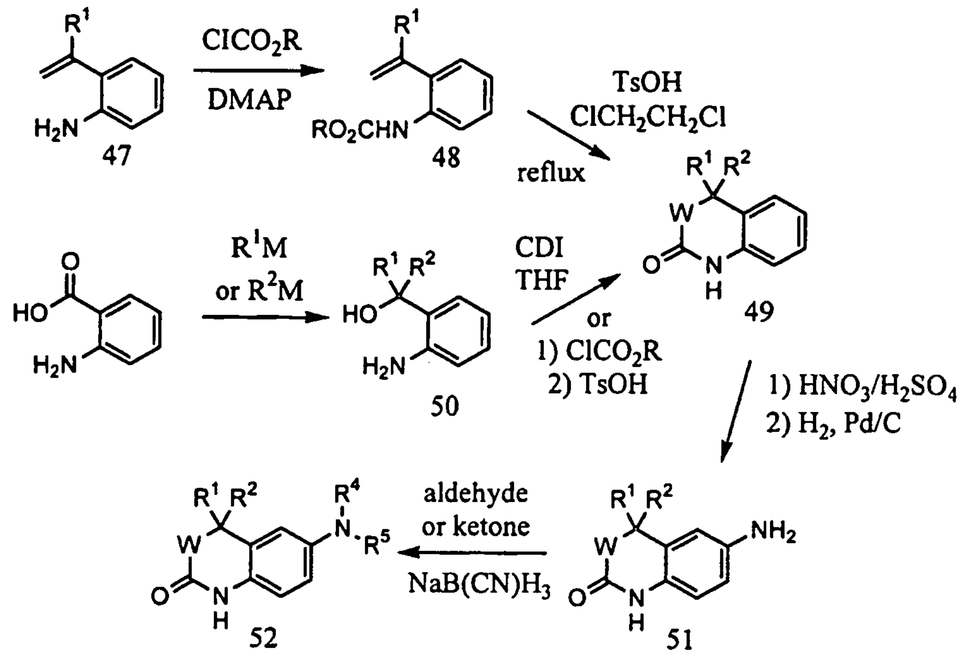
compound such as Structure **38** with trifluoroacetaldehyde in the presence of sodium cyanoborohydride followed by zinc reduction to provide an alkylated bis-amine compound such as Structure **39**. A typical Knorr procedure converts the alkylated amine compound **39** and ethyl 4,4,4-trifluoroacetoacetate to a quinolinone compound such as **40**. Reductive alkylation of compounds of **40** provides a bis-alkylaminoquinolinone such as Structure **41**. Treatment of compounds of Structure **41** with thiophenol affords 7-hydroxyquinolinone compounds such as **42**.

<u>Scheme VIII</u>



Scheme VIII describes the synthesis of 6-alkylaminocoumarins, as demonstrated by Structure **45**, from phenol through a similar route as that described in Schemes I and II. A mixture of a phenol compound and a 3-ketoester such as ethyl 4,4,4-trifluoroacetoacetate are heated in refluxing toluene in the presence of TsOH to afford a coumarin compound e.g., Structure **43**. Nitration of coumarin compounds (e.g., Structure **43**) followed by hydrogenation give aminocoumarin compounds such as Structure **44**. Sequential reductive alkylation provides dialkylamino-coumarin compounds as shown in Structure **45**. Hydrogenation of a dialkylamino-coumarin compound (e.g., Structure **45**) affords compounds Structure **46**.

Scheme IX

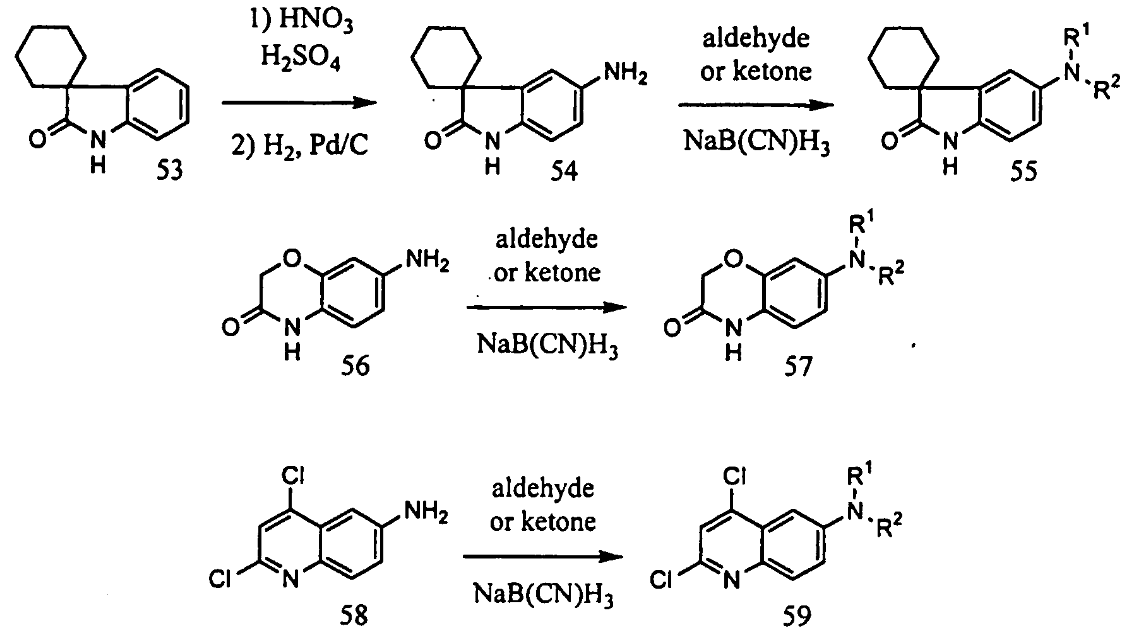


In another preferred embodiment, the syntheses of benzo-oxazinone compounds (e.g., Structure **49**) and derivatives thereof (e.g., Structures **51** and **52**) are shown in Scheme IX.

The process of Scheme IX begins with the treatment of an alkenylaniline compound such as Structure **47** with chloroformate in the presence of DMAP in THF to produce carbamates such as Structure **48**. Benzoxazinone compounds such as Structure **49** (W=O) are produced by p-tolylsulfonic acid catalyzed intra-molecular cyclization of a carbamate (e.g., Structure **48**).

An alternate synthesis of benzo-oxazinone compounds of Structure **49** is also shown in Scheme IX. In this synthetic route, carbon nucleophiles are added to 2-aminobenzoic acid to give the amino-alcohol compound **50**, which is converted to an aminobenzo-oxazinone compound such as Structure **49** by either 1,1'-carbonyldiimidazole in THF or the carbonate-cyclization route as described above. A classic nitration reaction of the aromatic benzoxazinone compound by nitric acid in concentrate sulfuric acid followed by palladium catalyzed hydrogenation produces amino compounds such as Structure **51**. A two-step sequential reductive alkylation as described previously produces dialkylamine-benzoxazinone compounds as shown in Structure **52**.

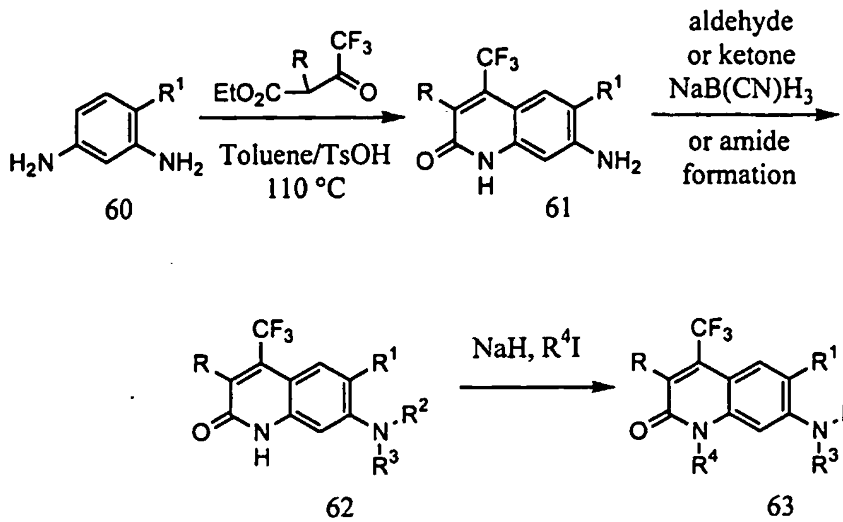
<u>Scheme X</u>



In another preferred embodiment, bioisosteres of 6-amino-2-quinolinones such as 5-amino-oxinole, 6-amino-benzoxazinone and quinoline compounds, which are useful AR and PR modulators, are prepared from a corresponding bicyclic compound. The bicyclic compounds such as Structures **53**, **56** and **58** are prepared by synthetic methods known to those skilled in the art.

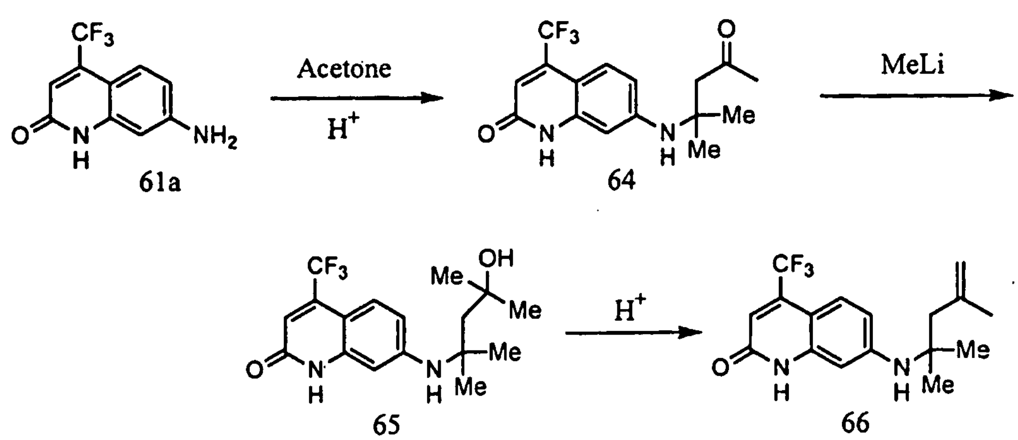
Scheme X describes a synthetic process for preparing 5-bisalkylamino-oxindole compounds such as Structure **55** and 6-bisalkylated compounds of Structures **57** and **59**. The method for preparing these compounds is described in Scheme IX and is analogous to the preparation of compounds such as Structure **52** from the corresponding quinolinone compound. The process involves sequential nitration, reduction and/or alkylation of the amine to produce compounds of Structures **55**, **57** and **59**.

<u>Scheme XI</u>



Scheme XI describes a preferred synthetic method to prepare 7-alkylamino-2-quinolinones such as Structure **63** via the Knorr reaction as previously described. The process of Scheme XI begins with a modified Knorr cyclization of 1,3-phenylenediamines of Structure **60** to give a 7-aminoquinolinone compound such as Structure **61**. A sequential reductive alkylation of Structure **61** in a similar process as that described in Scheme II affords compounds such as Structure **62**. Alkylation of quinolinone such as **62** with alkyl iodide in the presence of sodium hydride generates 1-alkyl quinolinone compounds such as Structure **63**.

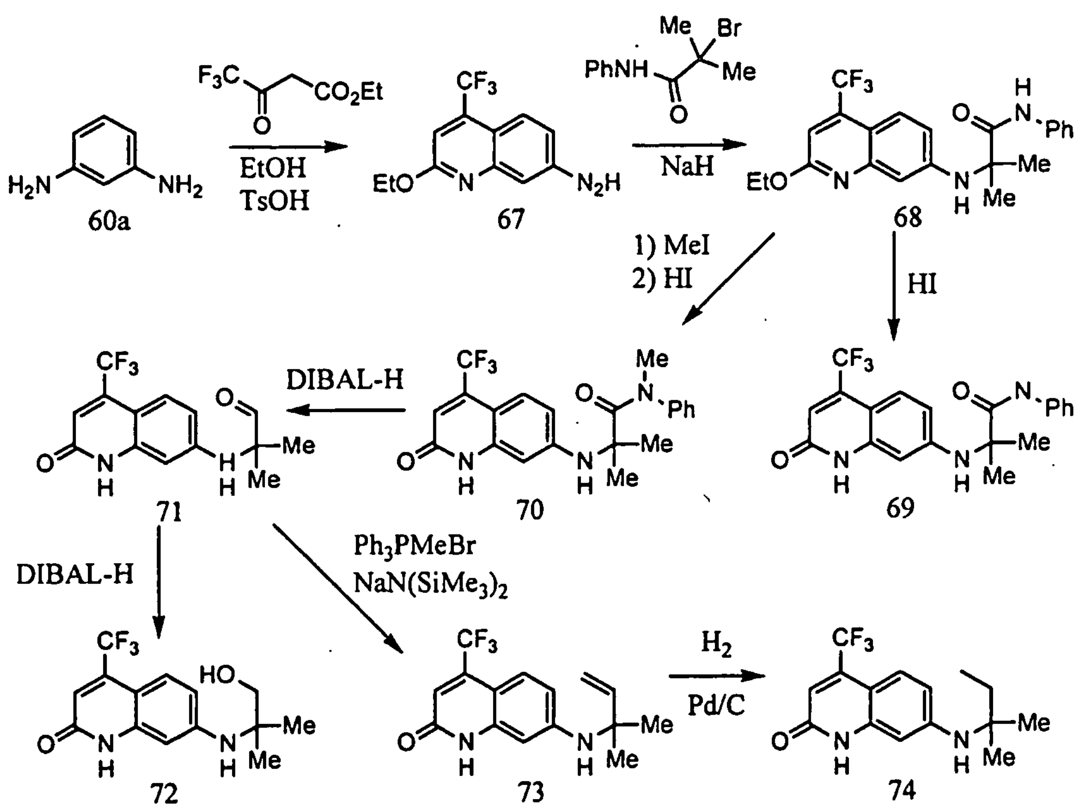
<u>Scheme XII</u>



In another preferred aspect of the invention, alkylamino-quinolinone compounds (e.g., Structure **66**) are prepared from a corresponding amino-quinolinone compound. Schemes XII, XIII and XIV describe the methods of introducing a quaternary carbon next to the amino position.

The process of Scheme XII begins with the treatment of a 7-aminoquinolinone such as Structure **61a** with acetic acid in acetone to afford an alkyl amino-quinolinone compound such as Structure **64**. Methyllithium addition to a compound such as Structure **64** in THF provides the corresponding alcohol adduct e.g., Structure **65**. An acid catalyzed dehydration of an amino alcohol compound such as **65** gives an alkene amino-quinolinone compound such as **66**.

Scheme XIII

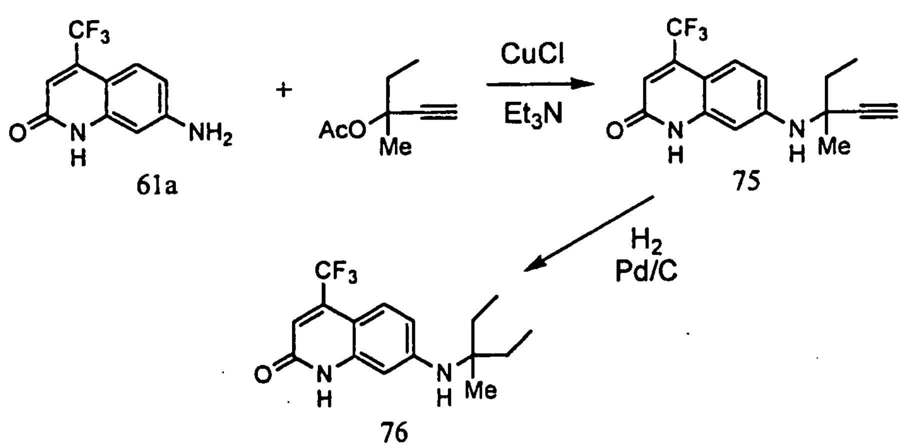


In another preferred reaction sequence, alkyl-quinolinones are produced by a Knorr cyclization of a diamine compound as previously described. Subsequent alkylation and oxidation produces alkyl-quinolinone compounds. The alkylamine-quinolinones may then be

further converted to various derivative compounds by reactions known to those skilled in the art as exemplified in the examples below.

Scheme XIII describes an alternate procedure to synthesize 2-quinolinones with a quaternary carbon adjacent to the 7-nitrogen. The process of Scheme XIII begins with a typical Knorr cyclization of a 1,3-phenylenediamine with a α-ketoester, ethyl 4,4,4-trifluoroacetoacetate, to afford an aminoquinoline compound such as **67** as a minor product. Alkylation of an aminoquinoline compound such as **67** with an amide such as N-phenyl-α-bromoisobutyramide in the presence of sodium hydride affords an alkylated quinoline product such as **68** in good yield. Hydrolysis of an alkylated quinoline compound (e.g., Structure **68**) with HI provides a 2-quinolinone such as **69**. Methylation of an alkylated quinoline compound such as **68** with iodomethane in the presence of sodium hydride followed by HI mediated hydrolysis produces a quinolinone such as Structure **70**. Reduction of an amide compound such as **70** with DIBAL-H affords an aldehyde compound such as **71** and an alcohol product such as **72**. Wittig reaction of aldehydes such as **71** affords olefins such as Structure **73**. Hydrogenation of an allylamino-quinolinone compound such as Structure **73** produces a corresponding alkylamino-quinolinone compound as shown in Structure **74**.

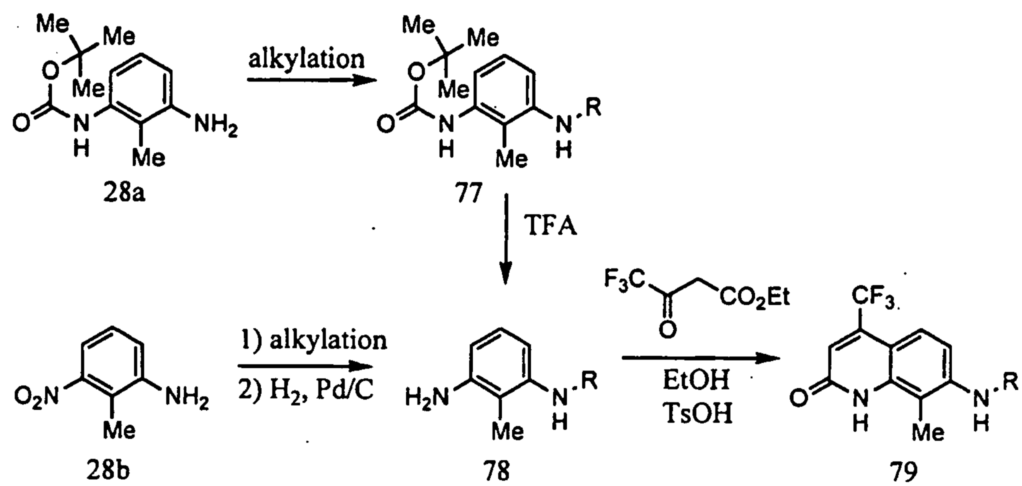
<u>Scheme XIV</u>



In another preferred aspect of the invention, alkylamino-quinolinone compounds are produced by copper chloride catalyzed substitution of an amino-quinolinone compound. Scheme XIV describes an alternate N-alkylation method for the preparation of alkylamino-quinolinone compounds. Treatment of an amino quinolinone compound such as **61a** and propargyl acetate

with copper chloride and a base such as triethylamine in THF affords alkylamine-quinolinone products such as **75**. Hydrogenation of an amino-acetylene compound such as **75** provides an alkylamino quinolinone compound as shown in Structure **76** in excellent yield.

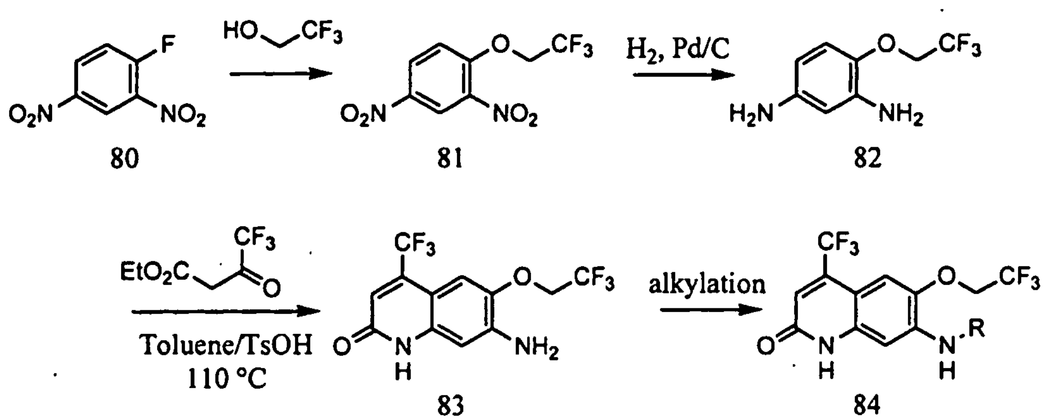
<u>Scheme XV</u>



Alkyl-diamino compounds (e.g. Structure **78**) are produced by two alternate synthetic methods in another preferred synthetic route as shown in Scheme XV. Alkylations of amino compounds as shown below are reactions known to those skilled in the art. The reaction as shown below is as an example of the preparation of these types of compounds.

The process of Scheme XV begins with alkylation of a mono-protected 1,3-phenylenediamine followed by trifluoroacetic acid (TFA) mediated de-protection to produce diamino compounds such as Structure **78**. Alternately, alkylation of a 3-nitroaniline followed by a reduction of the nitro group generates the same intermediates of Structure **78**. Knorr cyclization as previously described in the presence of a α-keto-ester such as ethyl 4,4,4-trifluoroacetoacetate affords compounds such as Structure **79** in good yield.

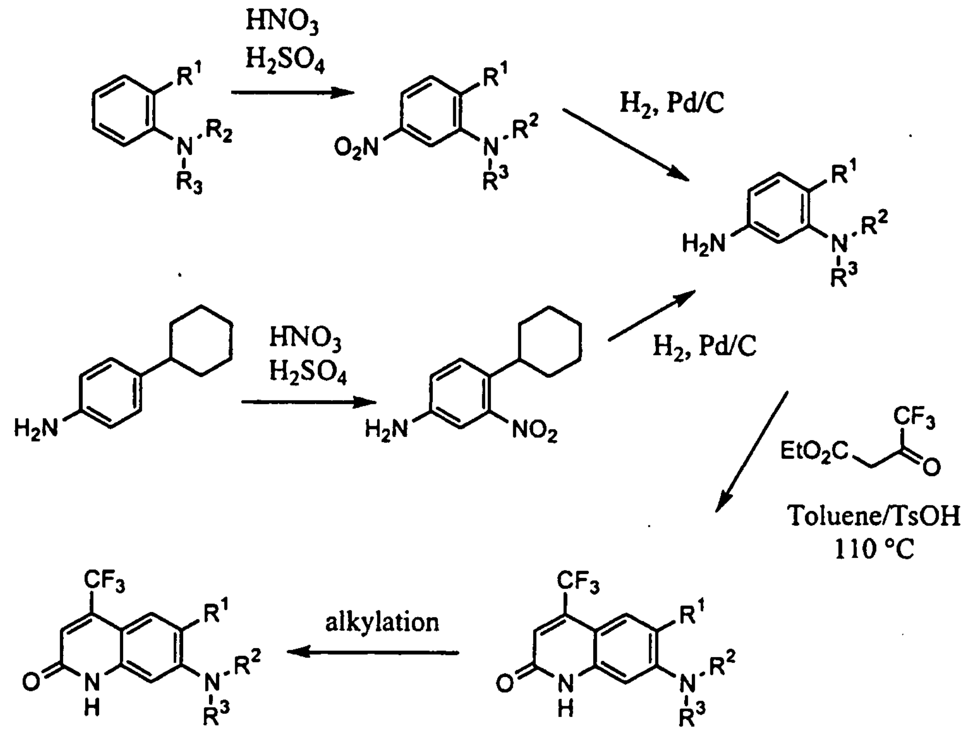
Scheme XVI



Substituted diamino compounds are produced in another preferred embodiment of the invention. The diamino compounds are then further reacted to produce quinolinone compounds via the Knorr reaction as previously described. Scheme XVI describes a synthetic process for producing alkoxy-alkylamino-quinolinone compounds such as Structure **84**.

The process starts with substitution of a bis-nitrofluorobenzene with 2,2,2-trifluoroethyanol in the presence of a base, such as sodium hydride to provide an alkoxy-nitrobenzene compound such as Structure **81**. Conversion of bis-nitro groups to bis-amino groups is accomplished by hydrogenation or metal reduction to give aniline compounds such as Structure **82**. A standard Knorr reaction with ethyl 4,4,4-trifluoroacetoacetate and p-tolylsufonic acid affords alkoxy-quinolinones such as Structure **83** in high yield. An alkoxy-amino-quinolinone compound such as **83** may subsequently be alkylated as previously described. For example, reductive alkylation of a compound such as Structure **83** with an aldehyde and sodium cyanoborohydride gives alkoxy-alkylamino-quinolinone compounds as shown in Structure **84**.

Scheme XVII

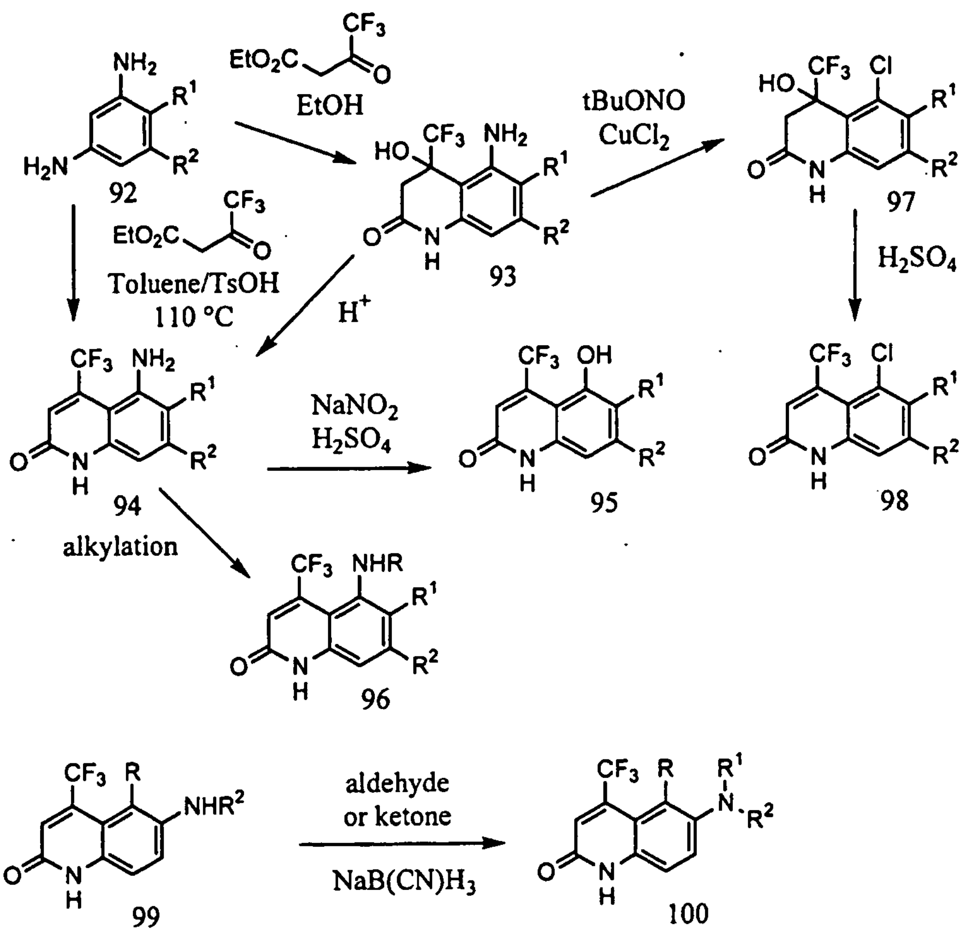


In another preferred reaction, substituted diamine compounds (e.g., Structure **87**) are produced by electrophilic aromatic substitution of activated aromatic amino-benzene rings. The substituted diamine compounds are then further reacted to produce quinolinone compounds (e.g., Structure **88**) and subsequent quinolinone derivatives thereof (e.g., Structure **89**) as previously described. Quinolinone compounds as shown in Scheme XVII are useful PR and AR modulators as described herein.

Scheme XVII describes processes to synthesize substituted alkylaminoquinolinone compounds such as **89**. Treatment of ortho-substituted aniline such as Structure **85** or a 4-substituted aniline such as **90** with nitric acid in concentrated sulfuric acid generates meta-nitrated products such as **86** or **91** in high yield. Hydrogenation of the nitro group on compounds such as **86** or **91** provides the Knorr precursors as shown as Structure **87**. Treatment of 1,3-phenylenediamines such as **87** with ethyl 4,4,4-trifluoroacetoacetate in refluxing toluene in the presence of a catalytic amount of acid, such as p-tolylsufonic acid, affords quinolinone

compounds as shown in Structure **88**. Additional alkylation at the 7-amino group provides more functionalized compounds such as Structure **89** as previously described.

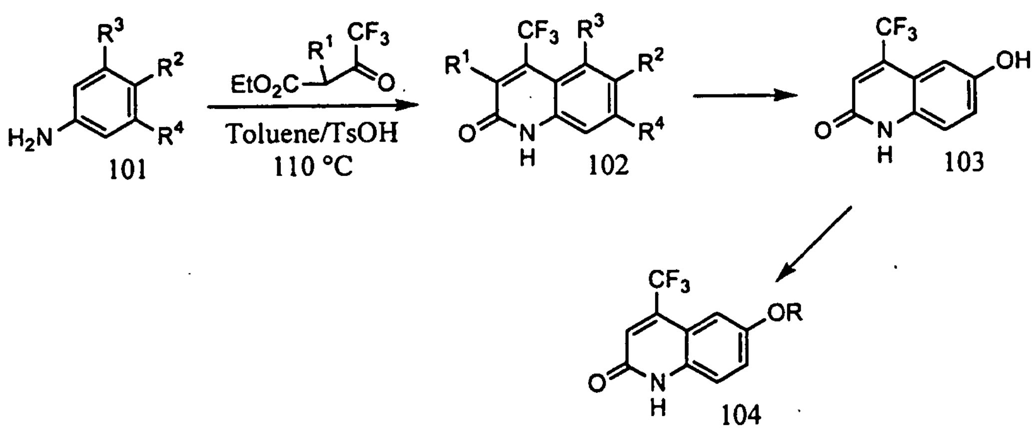
<u>Scheme XVIII</u>



In a preferred aspect of the invention, functionalized quinolinones or functionalized dihydro-quinolinones are prepared from the corresponding substituted diamino-benzene compound (e.g. Structure **92**). The amino portion of the quinolinone and dihydro-quinolinone compounds (e.g. Structures **94** and **93**), may then be converted to other functional groups by chemical reactions known to those skilled in the art. Examples of such conversions are demonstrated in Scheme XVIII, for example in the preparation of compounds such as **95**, **96**, **97** and **100**.

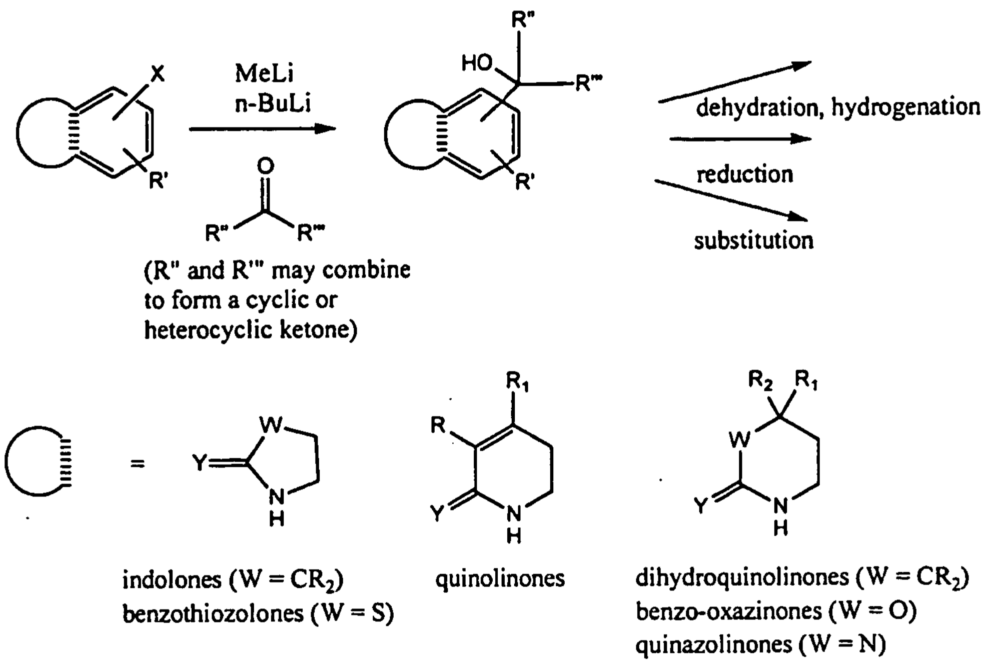
Scheme XVIII above describes methods of preparing functionalized quinolinones. The process of Scheme XVIII begins with modified Knorr reactions of diamine **92** with ethyl 4,4,4-trifluoroacetoacetate. In the p-tolylsufonic acid catalyzed refluxing toluene condition quinolinone compounds such as **94** are major products. In an alternate synthesis, the reaction is carried out in refluxing ethanol, which produces compounds such as Structure **93** as major products. Compounds such as **93** may then be converted to quinolinones such as **94** by acid catalyzed dehydration. The 5-amino group of compounds **93** or **94** is converted to 5-hydroxy derivatives of Structure **95** by diazotization-hydrolysis conditions using sodium nitrite and sulfuric acid. A similar condition by sodium nitrite and chloride converts the 5-amino to 5-chloro derivatives of Structure **98**. Reductive alkylation of compounds of Structures **94** and **99** affords compounds of Structures **96** and **100**.

<u>Scheme XIX</u>



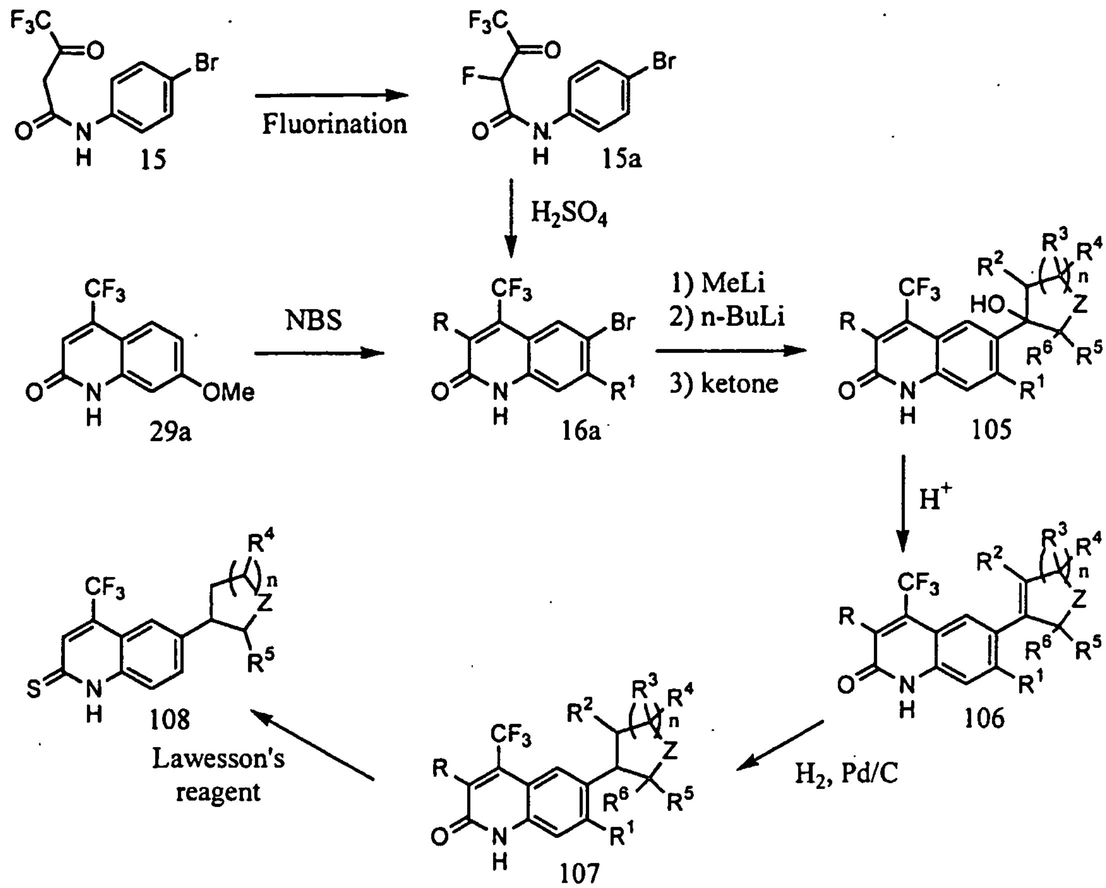
Another synthetic route into functionalized quinolinone compounds (e.g. Structures **102** and **104**) is shown in Scheme XIX. Scheme XIX describes the synthesis of substituted quinolinone compounds such as Structures **102** and **104** under similar Knorr reaction conditions as that described in Scheme I. The Knorr reaction may also be used on substituted aniline compounds (e.g. Structure **101**) to produce functionalized quinolinone compounds such as Structure **102**. The functionalized quinolinone compounds as shown above may then be converted to other functional groups to produce additional quinolinone derivatives such as compounds of Structure **104** as described herein.

Alkylated Aryl Compounds from Arylhalogens and Ketones



In another aspect of the invention, halogenated quinolinones, benzo-oxazinones, indolones, benzothiozolones, and quinazolinones (i.e., arylhalogen compounds) produce alkylated derivatives by a C-C coupling of the arylhalogen carbon and a ketone with a lithium reagent. The above reaction sequence depicts the conversion of arylhalogen compounds to arylalkyl compounds by reaction of the aryl halide compound with a ketone. Schemes XX through XXIX depict further examples of this type of functional group conversion and are provided to further illustrate the reaction with various ketones and aryl compounds.

Scheme XX

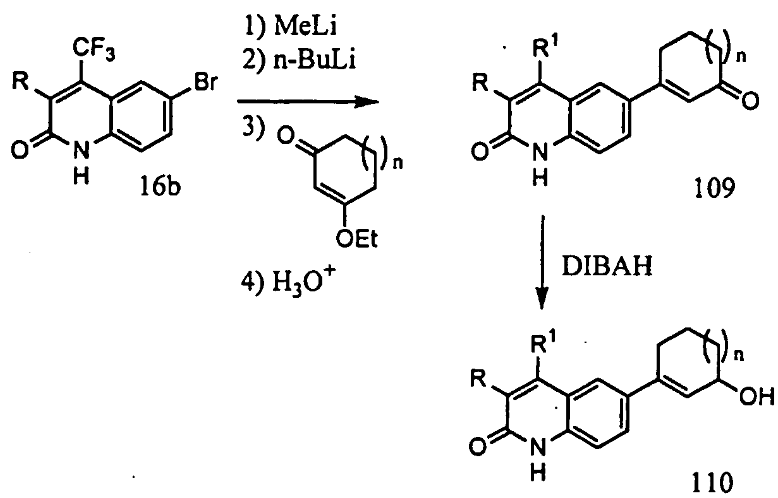


In another aspect of the invention, functionalized quinolinone compounds (e.g., Structure **105** and **109**) are produced by a C-C coupling of a halo-quinolinone such as Structure **16a** and a ketone as shown in Schemes XX and XXI. The halo-quinolinone may be produced by either of two synthetic routes as shown below in Scheme XX. Scheme XX describes the synthesis of a number of functionalized quinolinone compounds.

3-Fluorinated-quinolinone compounds such as Structure **16a** may be formed by treatment of a 3-ketoamide **15** with a fluorination reagent, such as fluorobenzenesulfonimide, to provide a fluorinated derivative product such as Structure **15a**, which is converted to the 3-fluoro quinolinone compound **16a** (R = fluorine) by the Knorr cyclization with concentrated sulfuric acid.

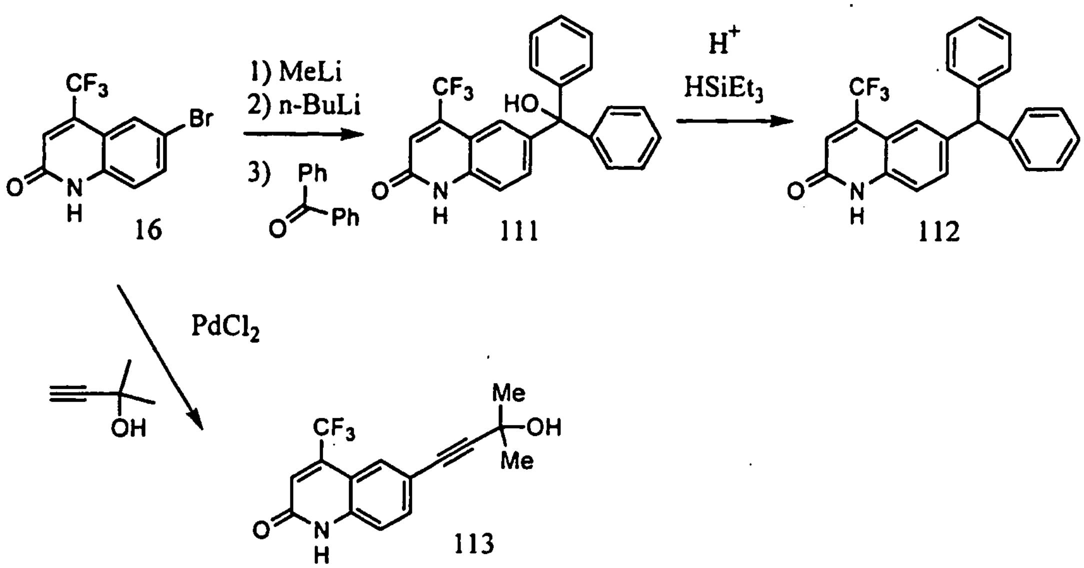
A 7-methoxy analogue of Structure **16a** is prepared by NBS bromination of quinolinone **29a**. Addition of a dianion generated from a bromo-quinolinone such as **16a** by two equivalents of base, such as alkyllithium, to a ketone affords the tertiary alcohols as shown in Structure **105**. Dehydration of an alcohol such as **105** with a catalytic amount of acid, such as sulfuric acid, gives olefins of Structure **106**. Subsequent hydrogenation of olefins such as **106** provides an alkyl-quinolinone such as Structure **107**. A thioquinolinone derivative may be synthesized by treatment of compounds **107** with Lawesson's reagent in toluene as previously described.

<u>**Scheme XXI**</u>



Scheme XXI describes a process of preparing alkenyl-quinolinone compounds. Addition of the dianion generated from a bromoquinolinone such as **16b** by methyllithium and n-butyllithium to a protected cyclic 1,3-diketone affords oxo-alkenyl-quinolinone compounds such as Structure **109** upon acid mediated hydrolysis of the adducts. Reduction of the oxo group on a compound such as **109** with DIBAH provides the alcohol derivative as shown in Structure **110**.

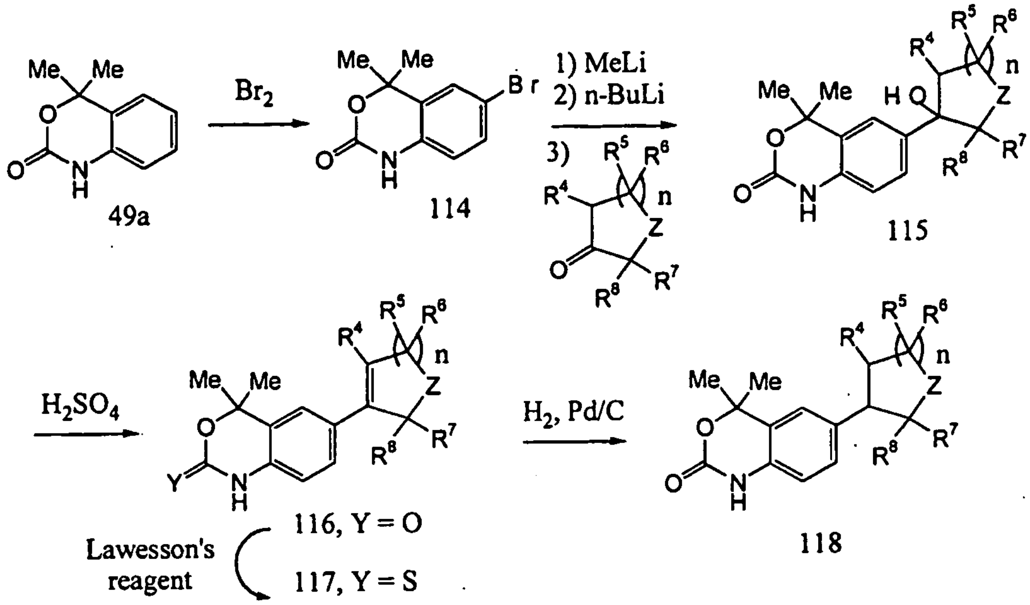
Scheme XXII



A further example of the conversion of arylhalogen compounds (e.g. Structure **16**) to arylalkyl compounds is shown in Scheme XXII. Scheme XXII describes the preparation of additional 6-alkyl 2-quinolinone compounds from the quinolinone dianion in a preferred aspect of the invention. Addition of a dianion generated from a bromo quinolinone, methyllithium and n-butyllithium to benzophenone gives an alkyl quinolinone such as compound **111**. Reduction of compound **111** with triethylsilane in the presence of an acid catalyst, such as TFA, affords an alkyl-quinolinone compound such as **112**.

In a further embodiment of the invention, aryl halogen compounds are converted to aryl alkynes by a palladium catalyzed coupling reaction between the aryl halogen (e.g., Structure **16**) and a terminal alkyne as shown above in Scheme XXII. For example, a palladium(II) catalyzed reaction of a bromoquinolinone such as **16** and a terminal alkyne such as dimethyl propargyl alcohol provides an alkynyl-quinolinone compound such as **113**.

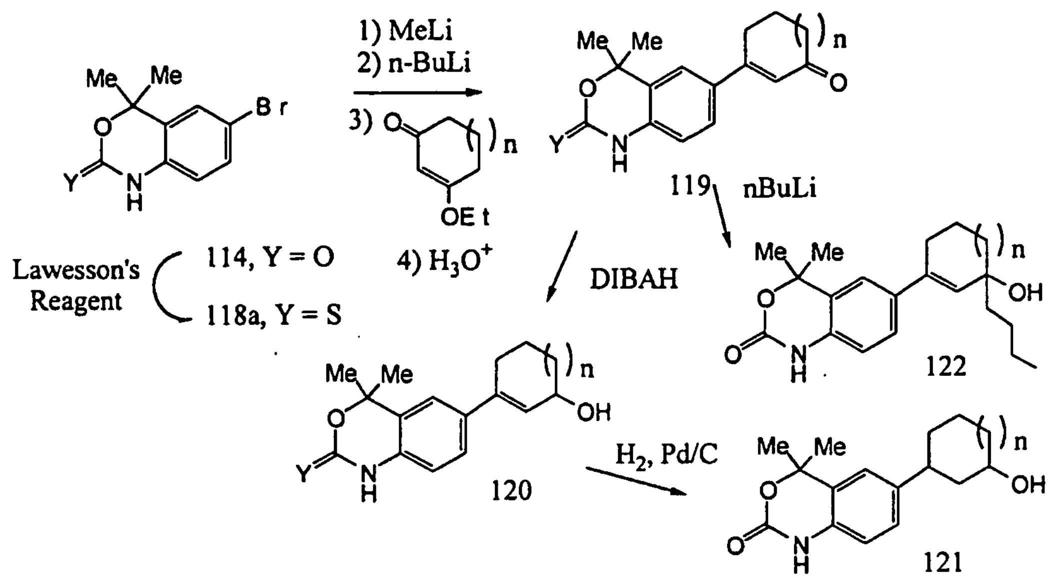
Scheme XXIII



A method of converting arylhalides to arylalkyl compounds is also employed with benzo-oxazinone compounds as shown in the above example. Scheme XXIII describes methods of synthesizing alkyl 1,3-benzo[d]oxazin-2-one compounds.

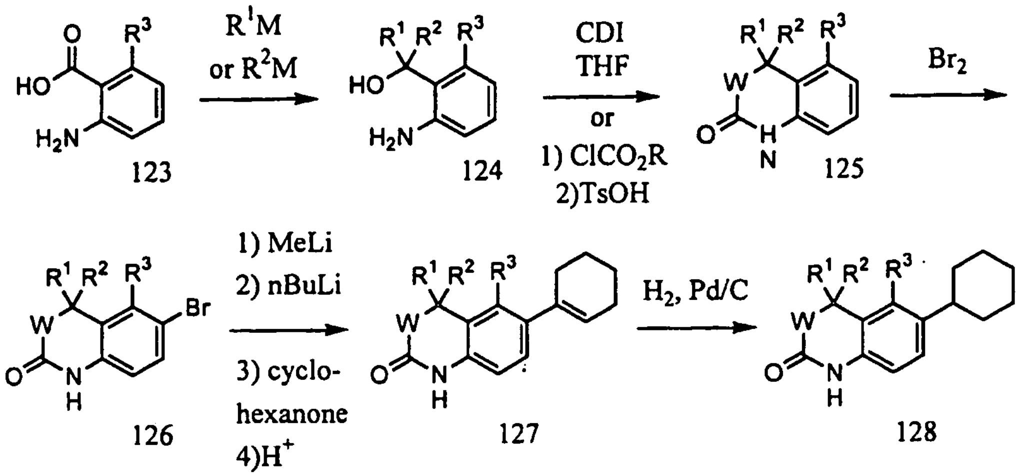
The process of Scheme XXIII begins with a bromination of a compound such as **49a** with bromine to give a bromobenzo-oxazinone compound such as **114**. Addition of the dianion generated from the lithiation of a compound such as **49a** to a ketone provides the hydroxy-alkyl adducts of Structure **115**. Dehydration of alcohol derivative **115** with a catalytic amount of sulfuric acid affords compounds such as Structure **116**, which may be hydrogenated to give compounds such as Structure **118**. Benzothiooxazinone compounds as shown in Structure **117** are prepared from the corresponding carbonyl compound (e.g., such as Structure **116**) by treatment with Lawesson's reagent as previously described.

Scheme XXIV



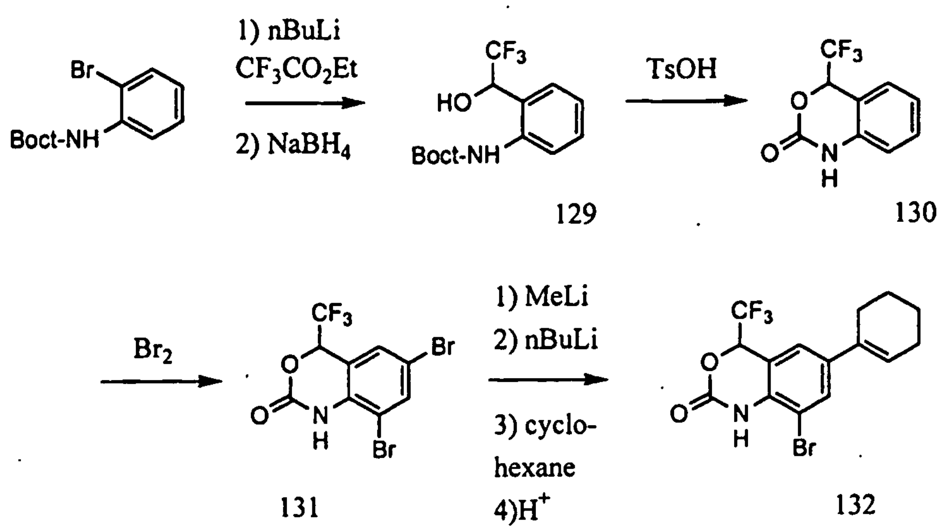
Scheme XXIV describes additional methods to prepare alkyl benzo-oxazinones. The process of Scheme XXIV begins with addition of the dianion generated from lithiation of compound **114** by alkyllithium to a protected 1,3-cyclodiketone. Hydrolysis of adducts with an acid affords alkene compounds Structure **119**. Addition of n-butyllithium to an enone such as **119** provides a tertiary alcohol such as **122**. Reduction of the enone **119** with DIBAL-H gives a secondary alcohol such as **120**. Hydrogenation affords compound such as **121**. Alkyl thio-benzo-oxazinone compounds are prepared by a similar process but using a thiobenzo-oxazinone such as **118a** in place of the oxo compound.

Scheme XXV



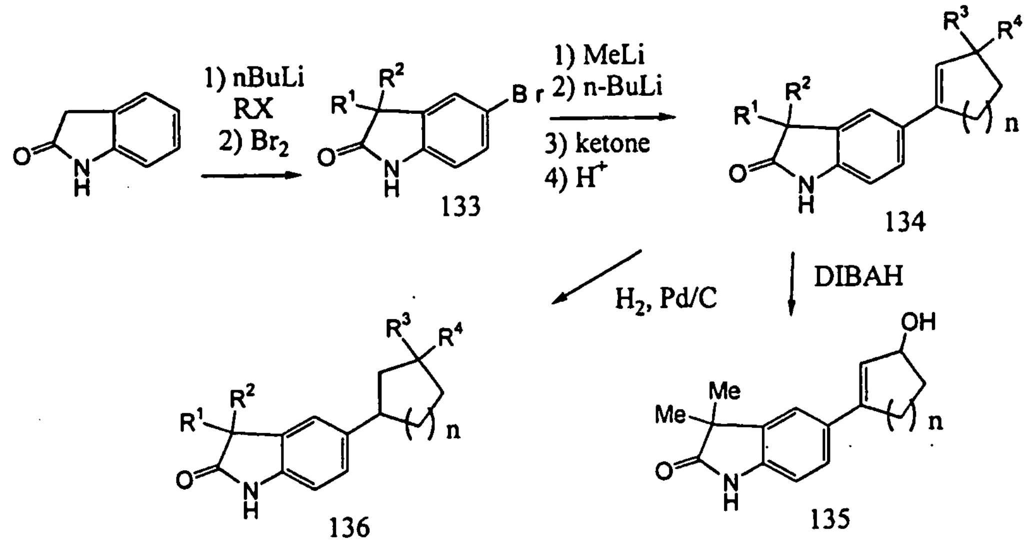
In another preferred aspect of the invention, substituted benzo-oxazinone compounds (e.g., Structure **125**) are prepared for an amino-benzoic acid and an organometallic reagent to form a hydroxy-aniline compound (e.g., Structure **124**) with either a halide or carbonyl diimidazole to form a benzo-oxazinone. The process of Scheme XXV begins with addition of either alkyl lithium or a Grignard reagent to a 2-aminobenzoic acid such as Structure **123** to generate amino alcohol compound such as Structure **124**. A previously described cyclization procedure from either 1,1'-carbonyldiimidazole treatment or acid catalyzed carbamate intermediate affords compounds such as Structure **125**. Treatment of benzo-oxazinone compounds (e.g., Structure **125**) with bromine provides brominated benzo-oxazinone compounds such as Structure **126**. Addition of an anion generated from compounds such as **126** and an alkyl lithium reagent to a ketone such as cyclohexanone affords compounds such as Structure **127**. The alkenyl-benzo-oxazinone compound (e.g., **127**) may be hydrogenated to give alkyl compounds such as Structure **128**.

<u>Scheme XXVI</u>



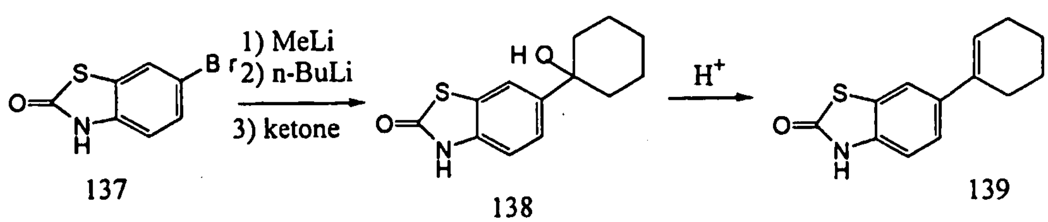
Scheme XXVI describes a process to introduce a trifluoromethyl group at the 4-position of benzo-oxazinone compounds. The process starts with addition of an N-protected 2-aminoaryl lithium generated by metal halogen exchange of 2-aminobromobenzene and n-butyllithium to ethyl trifluoroacetate followed by a reduction with sodium borohydride to provide compounds such as **129**. Acid catalyzed cyclization of compounds such as **129** afford benzo-oxazinone compounds such as **130**. The benzo-oxazinone compound may subsequently be treated with bromine to generate a bis-brominated product such as **131**. As previously described, the bromine may be substituted with an alkyl group. For example, the 6-cyclohexenyl derivative **132** is prepared in a similar fashion as that described in Scheme XXV.

Scheme XXVII



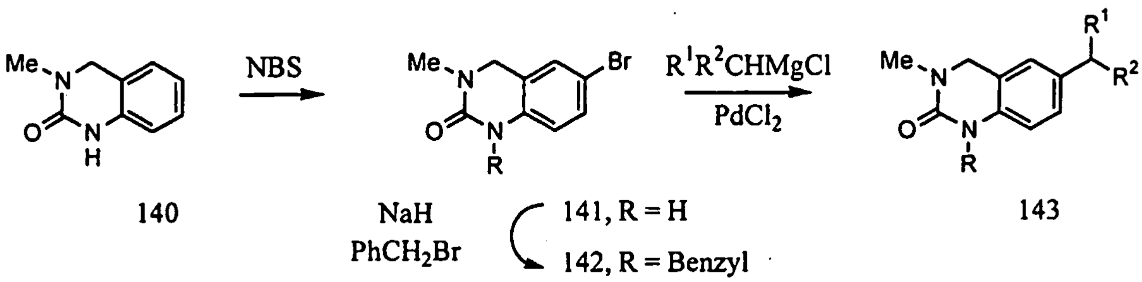
Scheme XXVII describes methods to prepare alkyl oxindole derivatives by bromination of the oxindole followed by substitution of the bromine group with an alkyl group as previously described. The process starts with alkylation of 2-indolone with alkyl halides in the presence of n-butyllithium followed by selective bromination to afford brominated oxindole compounds (e.g., Structure **133**). The alkyl-indolone compounds are prepared from a bromo compound such as **133** by a procedure similar to that as described in Scheme XXV.

Scheme XXVIII



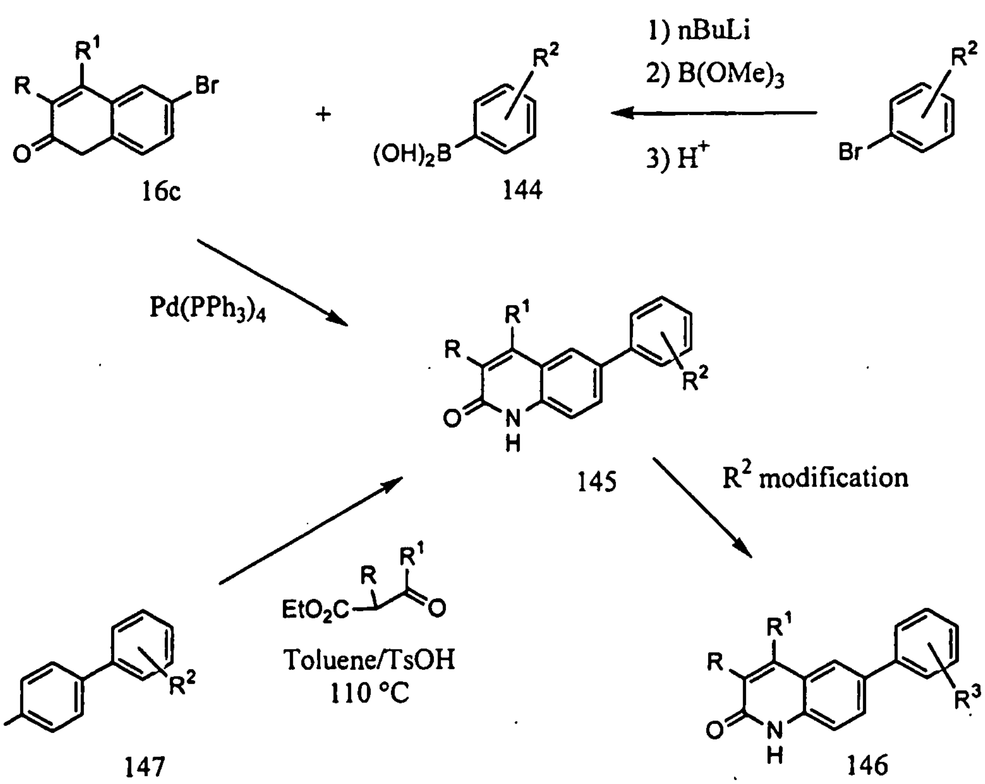
Scheme XXVIII describes a synthetic route of producing alkyl-benzothiozolones. The process is similar to that as described in Scheme XXV but using a halogenated benzothiozolone compound.

Scheme XXIX



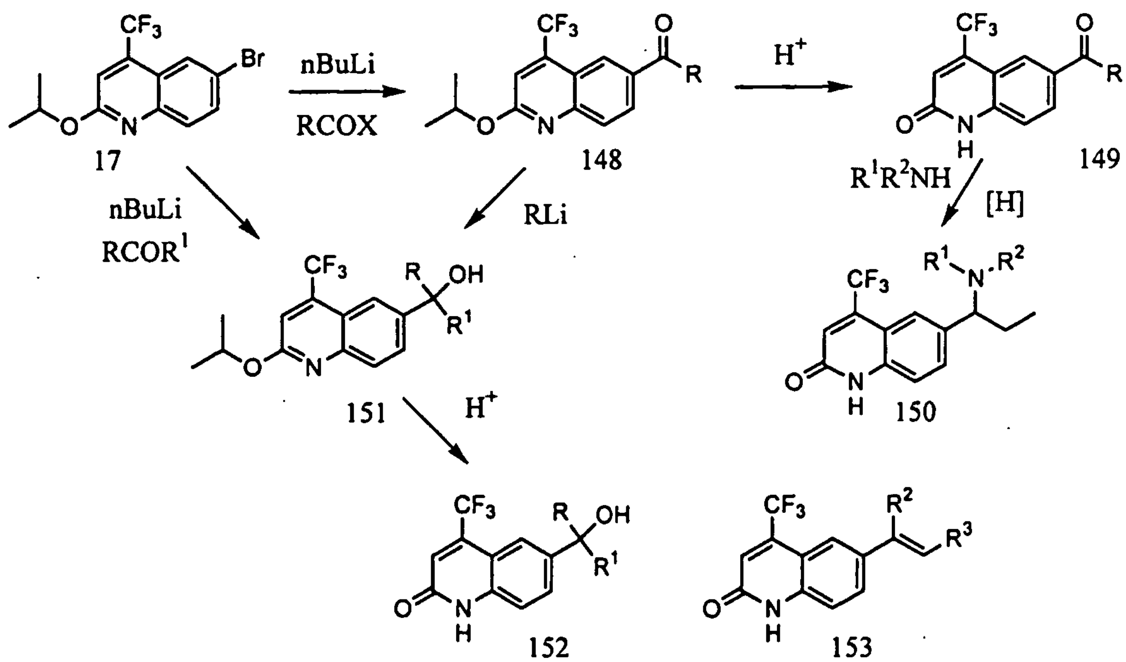
Scheme XXIX describes a process to prepare 2-quinazolinones. The process of Scheme XXIX begins with bromination of compound **140** to afford compound **141**, which is derivatized by treatment with benzyl bromide in the presence of sodium hydride to give compound **142**. A palladium catalyzed aromatic substitution of compounds of Structure **141** or **142** by Grignard reagents provides compounds of Structure **143**.

Scheme XXX



Scheme XXX describes an alternate method of preparing aryl-quinolinones by a modified Suzuki coupling reaction. The process starts with palladium catalyzed biaryl coupling of a bromo compound such as Structure **16c**, a brominated quinolinone, with an aryl boronic acid (e.g., Structure **144**). Aryl compounds such as Structure **145** are produced in this manner. The boronic acids of Structure **144** come from commercial sources or may be generated from aryl bromides by a standard three-step procedure which includes metal halogen exchange, addition to methyl borate and acidic work-up. Aryl substituted compounds of the present invention (e.g., Structure **145**) may be further functionalized by modification of the substituents on the aryl group by standard synthetic methods known to those skilled in the art. Alternately, aryl substituted compounds of the present invention such as Structure **145** may be prepared from the aryl aniline (e.g., 6-arylaniline, Structure **147**) as shown above by a Knorr reaction procedure as previously described.

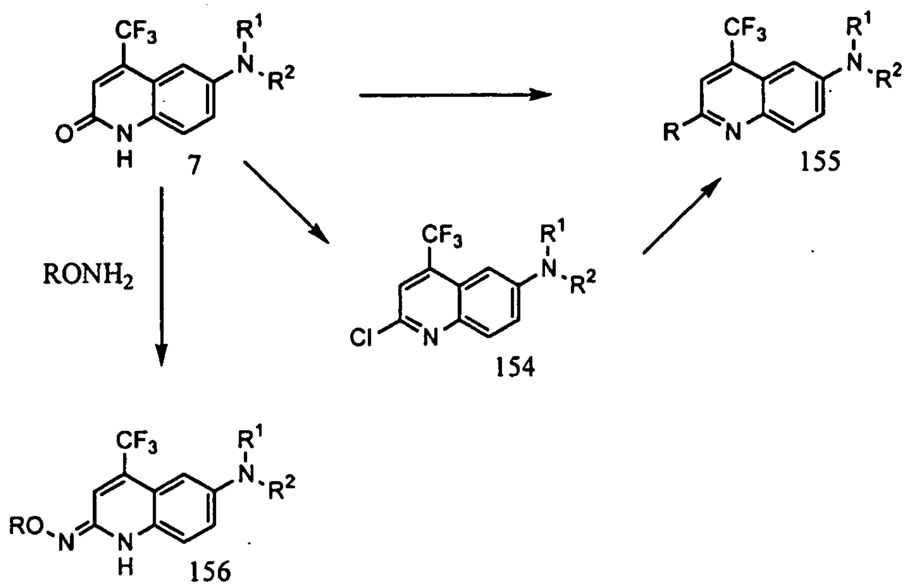
<u>Scheme XXXI</u>



Scheme XXXI describes additional methods to prepare 6-substituted 2-quinolinones such as Structures **149, 150, 152** and **153**. Lithiation of Structure **17** followed by addition to a Weinreb's amide afford compounds of Structure **148**. Hydrolysis of quinolines such as Structure

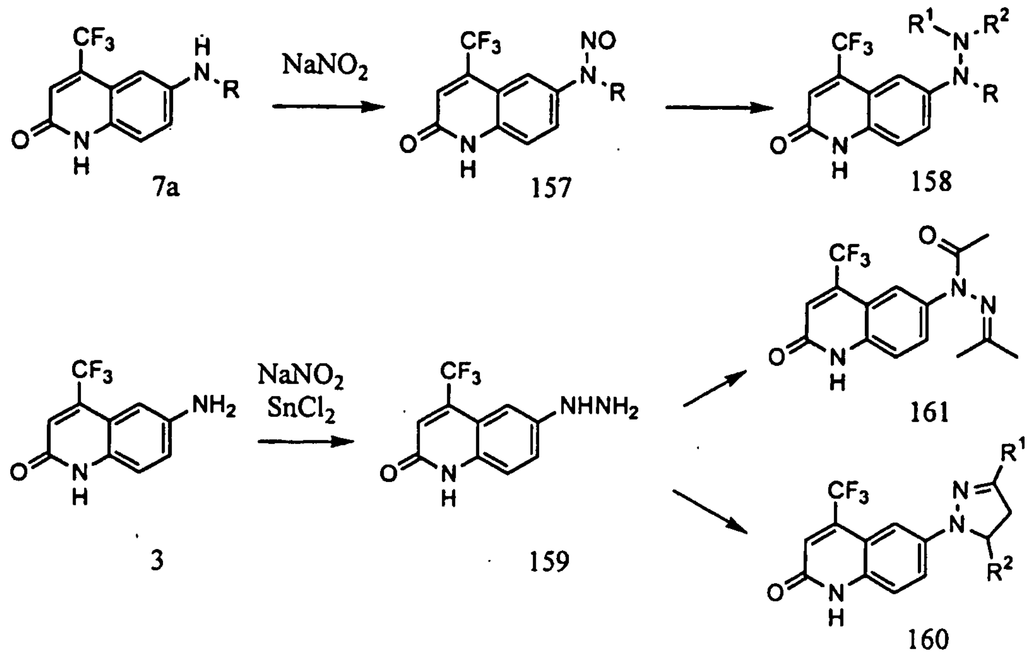
148 provides compounds of Structure **149**. Compounds of Structure **150** are obtained by reductive amination of compounds such as Structure **149**. Addition of a nucleophile to quinoline ketones of Structure **148** generates alcohols of Structure **151**, which are treated with acid to afford compounds of Structures **152** and **153**.

<u>**Scheme XXXII**</u>



Scheme XXXII describes the conversion of 2-quinolinones of Structure 7 to 2-substituted quinolines such as Structures **154, 155** and **156** by the chemical transformations known to those skilled in the art.

Scheme XXXIII



Scheme XXXIII describes methods to prepare compounds with a diazo containing side chain. Treatment of 6-aminoquinolinones such as Structure **7a** with $NaNO_2$ affords compounds of Structure **157**. Reduction of nitroso compounds such as Structure **157** followed by alkylation provide analogues of Structure **158**. Alkylation or acylation of hydrazine such as Structure **159** generates compounds of Structures **160** and **161**.

The compounds of the present invention also include racemates, stereoisomers and mixtures of said compounds, including isotopically labeled and radio-labeled compounds. Such isomers can be isolated by standard resolution techniques, including fractional crystallization and chiral column chromatography.

As noted above, any of the steroid modulator compounds of the present invention can be combined in a mixture with a pharmaceutically acceptable carrier to provide pharmaceutical compositions useful for treating the biological conditions or disorders noted herein in mammalian, and more preferably, in human patients. The particular carrier employed in these pharmaceutical compositions may take a wide variety of forms depending upon the type of administration desired, e.g., intravenous, oral, topical, suppository or parenteral.

In preparing the compositions in oral liquid dosage forms (e.g., suspensions, elixirs and solutions), typical pharmaceutical media, such as water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents and the like can be employed. Similarly, when preparing oral solid dosage forms (e.g., powders, tablets and capsules), carriers such as starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like will be employed. Due to their ease of administration, tablets and capsules represent the most advantageous oral dosage form for the pharmaceutical compositions of the present invention.

For parenteral administration, the carrier will typically comprise sterile water, although other ingredients that aid in solubility or serve as preservatives, may also be included. Furthermore, injectable suspensions may also be prepared, in which case appropriate liquid carriers, suspending agents and the like will be employed.

For topical administration, the compounds of the present invention may be formulated using bland, moisturizing bases, such as ointments or creams. Examples of suitable ointment bases are petrolatum, petrolatum plus volatile silicones, lanolin, and water in oil emulsions such as Eucerin™ (Beiersdorf). Examples of suitable cream bases are Nivea™ Cream (Beiersdorf), cold cream (USP), Purpose Cream™ (Johnson & Johnson), hydrophilic ointment (USP), and Lubriderm™ (Warner-Lambert).

The pharmaceutical compositions and compounds of the present invention will generally be administered in the form of a dosage unit (e.g., tablet, capsule etc.) at from about 1 μg/kg of body weight to about 500 mg/kg of body weight, more preferably from about 10 μg/kg to about 100 mg/kg, and most preferably from about 20 μg/kg to about 20 mg/kg. As recognized by those skilled in the art, the particular quantity of pharmaceutical composition according to the present invention administered to a patient will depend upon a number of factors, including, without limitation, the biological activity desired, the condition of the patient, and tolerance for the drug.

The compounds of this invention also have utility when radio- or isotopically-labeled as ligands for use in assays to determine the presence of AR or PR in a cell background or extract. They are particularly useful due to their ability to selectively activate androgen receptors or progesterone receptors, and can therefore be used to determine the presence of such receptors in the presence of other steroid receptors or related intracellular receptors.

Due to the selective specificity of the compounds of this invention for steroid receptors, these compounds can be used to purify samples of steroid receptors *in vitro*. Such purification can be carried out by mixing samples containing steroid receptors with one or more of the compounds of the present invention so that the compounds bind to the receptors of choice, and then separating out the bound ligand/receptor combination by separation techniques which are known to those of skill in the art. These techniques include column separation, filtration, centrifugation, tagging and physical separation, and antibody complexing, among others.

The compounds and pharmaceutical compositions of the present invention can advantageously be used in the treatment of the diseases and conditions described herein. In this regard, the compounds and compositions of the present invention will prove particularly useful as modulators of male sex steroid-dependent diseases and conditions such as the treatment of acne, male-pattern baldness, male hormone replacement therapy, wasting diseases, hirsutism, stimulation of hematopoiesis, hypogonadism, prostatic hyperplasia, osteoporosis (agonist), male contraception (agonist), impotence (agonist), cancer cachexia (agonist) various hormone-dependent cancers, including, without limitation, prostate and breast cancer and as anabolic agents.

The compounds and pharmaceutical compositions of the present invention possess a number of advantages over previously identified steroidal and non-steroidal compounds.

Furthermore, the compounds and pharmaceutical compositions of the present invention possess a number of advantages over previously identified steroid modulator compounds. For example, the compounds are extremely potent activators of AR, preferably displaying 50% maximal activation of AR at a concentration of less than 100 nM, more preferably at a concentration of less than 50 nM, more preferably yet at a concentration of less than 20 nM, and most preferably at a concentration of 10 nM or less. Also, the selective compounds of the present invention generally do not display undesired cross-reactivity with other steroid receptors, as is seen with the compound mifepristone (RU486; Roussel Uclaf), a known PR antagonist that displays an undesirable cross reactivity on GR and AR, thereby limiting its use in long-term, chronic administration. In addition, the compounds of the present invention, as small organic molecules, are easier to synthesize, provide greater stability and can be more easily administered in oral dosage forms than other known steroidal compounds.

The invention will be further illustrated by reference to the following non-limiting Examples.

EXAMPLE 1

6-Amino-4-trifluoromethyl-2(1H)-quinolinone (Compound **200**, Structure **3** of Scheme I)

N-(4-Acetylaminophenyl)-4,4,4-trifluoroacetoacetylamide hydrate (Compound **201**, Structure **2** of Scheme I):

In a 100 mL round bottom flask fitted with a reflux condenser, a mixture of 4-aminoacetanilide (Structure **1** of Scheme I) (7.5 g, 50 mmol), ethyl 4,4,4-trifluoroacetoacetate (17 g, 95 mmol, 1.9 equiv), nitrobenzene (30 mL), and water (2 mL, 0.11 mol) was heated in an oil bath at 130 °C for 1 h, then water (1 mL) was added and the mixture was heated at 130 °C for 2 h. After cooling to room temperature Et_2O (30 mL) was added to the solid mass and the solids were filtered and washed with Et_2O (3 × 30 mL), and dried under vacuum at 120 °C to give 12 g (85 %) of Compound **201** as a gray crystalline solid.

6-Amino-4-trifluoromethyl-2(*1H*)-quinolinone (Compound **200**, Structure **3** of Scheme I):

To a 50 mL r.b. flask charged with Compound **201** (3.6 g, 12 mmol) was added conc. H_2SO_4 (20 mL) and the dark brown mixture was heated in an oil bath at 95°C for 16 h. After cooling to room temperature the dark purple solution was poured onto crushed ice (50 g) and brought to pH~2 with conc. NaOH. EtOAc (50 mL) was added and the layers separated. The water layer was extracted with EtOAc (9 × 30 mL). The combined organic layers were washed with water and brine and dried over $MgSO_4$. Removal of solvent afforded 1.2 g of a bright yellow solid, which was purified by flash chromatography (silica gel, hexane:EtOAc 2:1 to 1:2 gradient) to give Compound **200** as a bright yellow solid (0.52 g, 18%): ^{1}H NMR (500 MHz, acetone-d_6) 10.9 (bs, 1 H), 7.31 (d, J = 9.3, 1 H), 7.10 (dd, J = 9.3, 2.4, 1 H), 7.04 (t, J = 2.4, 1 H), 6.85 (s, 1 H), 4.91 (bs, 2 H).

6-Amino-4-trifluoromethyl-2(*1H*)-quinolinone (Compound **200**, Structure **3** of Scheme I) was also prepared by the following General Procedures I-III from aniline:

4-Trifluoromethyl-2(*1H*)-quinolinone (Compound **202**, Structure **5** of Scheme I):

General Procedure I (Synthesis of 2(1*H*)-quinolinone from aniline):

A solution of aniline in benzene or toluene (2-10 mL/mmol) and an acetoacetate derivative (1.2 equiv) was heated at reflux for 12-48 hrs. The resulting mixture was cooled to room temperature and concentrated under reduced pressure. The crude reaction mixture was diluted in concentrated sulfuric acid (8 mL/mmol) and heated to 80-100° C for 6-16 hrs. The resulting mixture was poured over ice and neutralized with 6 M NaOH solution to pH 7.0, extracted with CH_2Cl_2 (3 x 30 mL/mmol), washed with pH 7 phosphate buffer (50 mL/mmol) and brine (50 mL/mmol). The organic solution was dried ($MgSO_4$) and concentrated under reduced pressure. Purification was performed either by flash chromatography (silica gel, 20:1, CH_2Cl_2/MeOH) or by crystallization to afford the desired quinolinone as a fluorescent-yellow solid.

Alternatively, a mixture of aniline and a 3-ketoester such as ethyl 4,4,4-trifluoroacetoacetate (1.2 equiv) in toluene (0.1-0.5 M) was heated at reflux for 24 h until the starting material was completely consumed by TLC. A catalytic amount of p-tolylsulfonic acid (1-10%) was added and the mixture was refluxed for additional 24 h. Similar work-up as described above afforded Compound **202** as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.25 (bs, 1 H), 7.70 (d, J = 8.0, 1 H), 7.65 (t, J = 8.0, 1 H), 7.44 (d, J = 8.0, 1 H), 7.32 (t, J = 8.0, 1 H), 6.99 (s, 1 H).

6-Nitro-4-trifluoromethyl-2(*1H*)-quinolinone (Compound **203**, Structure **6** of Scheme I): General Procedure II (Nitration reaction):

To solution of a 2(1*H*)-quinolinone, such as Compound **202**, in conc. H_2SO_4 (0.2-1.0 M) at room temperature was added HNO_3 (1.0 equiv). The reaction mixture was stirred for 10 min and was poured into ice water. The mixture was neutralized to PH~7 and extracted with EtOAc. Recystallization provided Compound **203** as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 12.82 (bs, 1 H), 8.47 (dd, J = 9.5, 2.5, 1 H), 8.44 (m, 1 H), 7.59 (d, J = 9.5, 1 H), 7.21 (s, 1 H).

6-Amino-4-trifluoromethyl-2(*1H*)-quinolinone (Compound **200**, Structure **3** of Scheme I) General Procedure III (Hydrogenation reaction):

Compound **203** in EtOAc (0.2-1.0 M) was hydrogenated with a hydrogen balloon in the presence of 5% or 10% Pd/C (1-5 mol%). Filtration from the catalyst on Celite afforded Compound **200** as yellow solid.

EXAMPLE 2

6-Propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **204**, Structure 7 of Scheme II, where R^1 = H, R^2 = propyl)

This compound was prepared from Compound **200** and propionaldehyde by the following General Procedure IV (Reductive alkylation of amine by aldehyde):

To a solution of Compound **200** (Structure **3** of Scheme II) (35 mg, 0.15 mmol) in methanol (20 mL) was added a propionaldehyde (2-5 equiv) followed by $NaCNBH_3$ (2-5 equiv). The mixture was stirred at room temperature for 4 h and water (20 mL) was added. The water layer was extracted with EtOAc (2x 20 mL) and the combined organic layers were washed with brine and dried over $MgSO_4$. Concentration and purification by flash chromatography (silica gel, hex/EtOAc 3:1) afforded Compound **204** as a yellow solid (70-95%): ^{1}H NMR (500 MHz, $CDCl_3$) 11.2 (bs, 1 H), 7.22 (d, J = 8.8, 1 H), 7.05 (s, 1 H), 6.96 (dd, J = 8.8, 2.4, 1 H), 6.88 (s, 1 H), 3.77 (t, J = 4.4, 1 H), 3.12 (dt, J = 7.5, 4.4, 2 H), 1.72-1.63 (m, 2 H), 1.04(t, J = 7.3, 3 H).

EXAMPLE 3

6-Isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **205**, Structure 7 of Scheme II, where R^1 = H, R^2 = isopropyl)

This compound was prepared from Compound **200** and acetone by the following General Procedure V (Reductive alkylation of amine by ketone):

To a solution of Compound **200** (Structure **3** of Scheme II) (35 mg, 0.15 mmol) in 10 mL MeOH was added acetone (0.5 mL, excess) followed by $NaCNBH_3$ (30 mg, 0.50 mmol) and AcOH (0.5 mL). The mixture was stirred at room temperature for 1h and 10 mL water was added. The water layer was extracted with EtOAc (2 x 15 mL) and the combined organic layers were washed with brine and dried over $MgSO_4$. Concentration and purification by flash chromatography (silica gel, hex/EtOAc 2:1) afforded 33 mg (81 %) of Compound **205** as a bright yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 10.9 (bs, 1H), 7.33 (d, J = 8.8, 1 H), 7.08 (dd, J = 8.8, 2.4, 1 H), 6.87 (t, J = 2.4, 1 H), 6.86 (s, 1 H), 5.00 (d, J = 6.8, 1 H), 3.70-3.63 (m, 1 H), 1.23 (d, J = 6.9, 6 H).

EXAMPLE 4

6-Isobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 206, Structure 7 of Scheme II, where R^1 = H, R^2 = isobutyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using isobutyraldehyde in place of propionaldehyde. Compound **206** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.1 (bs, 1 H), 7.20 (d, *J* = 8.8, 1 H), 7.04 (s, 1 H), 6.95 (dd, *J* = 8.8, 2.4, 1 H), 6.87 (s, 1 H), 3.83 (bs, 1 H), 2.97 (t, *J* = 6.3, 1 H), 1.95-1.89 (m, 1 H), 1.02 (d, *J* = 6.8, 6 H).

EXAMPLE 5

6-(2,2-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 207, Structure 7 of Scheme II, where R^1 = H, R^2 = 2,2-dimethylpropyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using trimethylacetaldehyde in place of propionaldehyde. Compound **207** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 10.4 (bs, 1 H), 7.14 (d, *J* = 8.8, 1 H), 7.03 (s, 1 H), 6.97 (dd, *J* = 8.8, 2.4, 1 H), 6.90 (s, 1 H), 3.79 (t, *J* = 5.9, 1 H), 2.94 (d, *J* = 5.9, 2 H), 1.03 (s, 9 H).

EXAMPLE 6

6-Cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 208, Structure 7 of Scheme II, where R^1 = H, R^2 = cyclopentyl)

This compound was prepared in a similar fashion as that described in Example 3, General Procedure V but using cyclopentanone in place of acetone. Compound **208** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 10.9 (bs, 1 H), 7.32 (d, *J* = 8.8, 1 H), 7.08 (dd, *J* = 8.8, 2.4, 1 H), 6.87 (t, *J* = 2.4, 1 H), 6.85 (s, 1 H), 5.21 (d, *J* = 6.4, 1 H), 3.84-3.81 (m, 1 H), 2.04-2.00 (m, 2 H) 1.76-1.71 (m, 2 H), 1.67-1.59 (m, 2 H), 1.58-1.52 (m, 2 H).

EXAMPLE 7

6-(2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **209**, Structure **7** of Scheme II, where R^1 = H, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using trifluoroacetaldehyde in place of propionaldehyde. Compound **209** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.05 (s, 1 H), 7.36 (d, J = 8.7, 1 H), 7.09 (s, 1 H), 7.04 (d, J = 8.7, 1 H), 7.02 (s, 1 H), 4.10 (t, J = 6.9, 1 H), 3.86-3.78 (m, 2 H).

EXAMPLE 8

6-(2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **210**, Structure **7** of Scheme II, where R^1 = H, R^2 = 2,2,3,3,3-pentafluoropropyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using pentafluoropropyraldehyde in place of propionaldehyde. Compound **210** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 12.2 (bs, 1 H), 7.35 (d, J = 8.8, 1 H), 7.09 (s, 1 H), 7.05 (dd, J = 8.8, 2.4, 1 H), 7.03 (s, 1 H), 4.05 (t, J = 6.8, 1 H), 3.91-3.84 (m, 2 H).

EXAMPLE 9

6-(2,2-Difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **211**, Structure **7** of Scheme II, where R^1 = H, R^2 = 2,2-difluoroethyl)

This compound was prepared from Compound **200** and difluoroacetic acid by the following General Procedure VI (Reductive alkylation of amine by acid):

To a solution of an aniline such as Compound **200** (Structure **3** of Scheme II) in an acid such as difluoroacetic acid as solvent was added sodium borohydride (excess) slowly, the resulting mixture was stirred at room temperature for several hours until the reaction went completion by TLC (addition of additional sodium borohydride or at elevate temperature would result in the formation of bis-alkylated product). The reaction was quenched by 10% NaOH and extracted with EtOAc (2x). Removal of solvent and chromatography of the crude residue afforded the N-alkylated product.

Compound **211** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.37 (d, J = 8.8, 1 H), 7.09 (s, 1 H), 7.03 (dd, J = 2.5, 8.9, 1H), 6.97 (s, 1 H), 5.97 (tt, J = 3.9, 55.8, 1 H), 4.03 (t, J = 6.8, 1 H), 3.65-3.55 (m, 2 H).

EXAMPLE 10

6-(2-Chloro-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 212, Structure 7 of Scheme II, where R^1 = H, R^2 = 2-chloro-2,2-difluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using chlorodifluoroacetic acid in place of difluoroacetic acid. Compound **212** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.38 (d, *J* = 8.7, 1 H), 7.09 (s, 1 H), 7.08-7.05 (m, 2 H), 4.26 (t, *J* = 6.8, 1 H), 3.99-3.92 (m, 2 H).

EXAMPLE 11

6-Acetylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 213, Structure 7 of Scheme II, where R^1 = H, R^2 = acetyl)

This compound was prepared from Compound **200** and acetic anhydride by the following General Procedure VII (Acylation of amine):

To a solution of an amine such as Compound **200** (Structure **3** of Scheme II) in methylene chloride (0.1-0.5 M) was added an acid chloride or anhydride (1.5 equiv) and triethylamine (1.5 equiv) and the resulting mixture was stirred at room temperature for 1 h till the reaction went completion. The mixture was quenched with water and extracted with EtOAc. Removal of solvent and chromatography afforded the amide in good yield. Compound **213** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 11.0 (bs, 1 H), 9.4 (bs, 1 H), 8.23 (s, 1 H), 7.91 (dd, *J* = 8.8, 2.4, 1 H), 7.46 (d, *J* = 8.8, 1 H), 6.93 (s, 1 H), 2.11 (s, 3 H).

EXAMPLE 12

6-Trifluoroacetylamino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 214, Structure 7 of Scheme II, where R^1 = H, R^2 = trifluoroacetyl)

This compound was prepared in a similar fashion as that described in Example 11, General Procedure VII but using trifluoroacetic anhydride in place of acetic anhydride. Compound **214** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 11.2 (bs, 1 H), 10.5 (bs, 1 H), 8.25 (t, *J* = 2.0, 1 H), 8.04 (dd, *J* = 8.8, 2.4, 1 H), 7.58 (d, *J* = 8.8, 1 H), 7.00 (s, 1 H).

EXAMPLE 13

6-Benzoylamino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **215**, Structure 7 of Scheme II, where R^1 = H, R^2 = benzoyl)

This compound was prepared in a similar fashion as that described in Example 11, General Procedure VII but using benzoyl chloride in place of acetic anhydride. Compound **215** was isolated as a yellow solid: ^{1}H NMR (500 MHz, DMSO-d_6) 12.3 (bs, 1 H), 10.5 (bs, 1 H), 8.38 (s, 1 H), 8.06 (dd, J = 8.8, 0.9, 1 H), 7.98 (d, J = 6.8, 2 H), 7.62-7.59 (m, 1 H), 7.56-7.53 (m, 2 H), 7.43 (d, J= 8.8, 1 H), 7.00 (s, 1 H).

EXAMPLE 14

6-Dimethylacetylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **216**, Structure 7 of Scheme II, where R^1 = H, R^2 = dimethylacetyl)

This compound was prepared in a similar fashion as that described in Example 11, General Procedure VII but using isobutyric anhydride in place of acetic anhydride. Compound **216** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 11.1 (bs, 1 H), 9.3 (bs, 1 H), 8.30 (t, J = 1.9, 1 H), 7.95 (dd, J = 8.8, 2.4, 1 H), 7.47 (d, J = 8.8, 1 H), 6.94 (s, 1 H), 2.68-2.62 (m, 1H) 1.19 (d, J = 6.8, 6 H).

EXAMPLE 15

6-Dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **217**, Structure 7 of Scheme II, where R^1 = R^2 = methyl)

This compound was prepared from Compound **200** and formaldehyde by the following General Procedure VIII (Dialkylation of amine):

To a solution of Compound **200** (Structure **3** of Scheme II) (35 mg, 0.15 mmol) in methanol (20 mL) was added an aldehyde (2-5 equiv) followed by $NaCNBH_3$ (2-5 equiv). The mixture was stirred at room temperature for 4 h and water (20 mL) was added. The water layer was extracted with EtOAc (2x 20 mL) and the combined organic layers were washed with brine and dried over $MgSO_4$. Concentration and purification by flash chromatography (silica gel, hex/EtOAc 3:1) afforded the mono-alkylated product as a yellow solid (70-95%). Repeating the same procedure in the presence of the second aldehyde or ketone afforded the dialkylated product (50-90%). In case that both alkyl groups were same, the double alkylation was carried

out in one step, in which a catalytic amount of acetic acid was needed to accelerate the reaction. The acetic acid was also needed when a ketone was used as an alkylating agent.

Compound **217** was isolated as a bright yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 10.9 (bs, 1 H), 7.42 (d, J = 9.3, 1 H), 7.28 (dd, J = 9.3, 2.9, 1 H), 6.94 (s, 1 H), 6.89 (s, 1 H), 2.99 (s, 6 H).

EXAMPLE 16

6-Diethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 218, Structure 7 of Scheme II, where $R^1 = R^2$ = ethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetaldehyde in place of paraformaldehyde. Compound **218** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 10.3 (bs, 1 H), 7.18 (d, J = 9.3, 1 H), 7.07 (dd, J = 9.3, 2.4, 1 H), 7.03 (s, 1 H), 6.95 (s, 1 H), 3.39 (q, J = 6.8, 4 H), 1.18 (t, J = 6.8, 6 H).

EXAMPLE 17

6-Dipropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 219, Structure 7 of Scheme II, where $R^1 = R^2$ = propyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using propionaldehyde in place of paraformaldehyde. Compound **219** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.0 (bs, 1 H), 7.22 (d, J = 9.3, 1 H), 7.03 (dd, J = 9.3, 2.4, 1 H), 7.03 (s, 1 H), 6.90 (s, 1 H), 3.28 (t, J = 7.3, 4 H), 1.66-1.58 (m, 4 H), 0.95 (t, J = 7.3, 6 H).

EXAMPLE 18

6-Dibutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 220, Structure 7 of Scheme II, where $R^1 = R^2$ = butyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using butyraldehyde in place of paraformaldehyde. Compound **220** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 12.2 (bs, 1 H), 7.32 (d, J = 8.8, 1 H), 7.06 (dd, J = 8.8, 2.4, 1 H), 7.04 (s, 1 H), 6.90 (s, 1 H), 3.31 (t, J = 6.8, 4 H), 1.60-1.50 (m, 4 H), 1.41-1.33 (m, 4 H), 0.97 (t, J = 7.3, 6 H).

EXAMPLE 19

6-Diisobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **221**, Structure 7 of Scheme II, where $R^1 = R^2$ = isobutyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using isobutyraldehyde in place of paraformaldehyde. Compound **221** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.7 (bs, 1 H), 7.27 (d, J = 9.3, 1 H), 7.06 (dd, J = 9.3, 2.9, 1 H), 7.04 (s, 1 H), 6.90 (s, 1 H), 3.18 (d, J = 6.8, 3 H), 2.09-2.02 (m, 2 H), 0.92 (d, J = 6.3, 12 H).

EXAMPLE 20

6-(bis-Cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **222**, Structure 7 of Scheme II, where $R^1 = R^2$ = cyclopropylmethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using cyclopropanecarboxaldehyde in place of paraformaldehyde. Compound **222** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.5 (bs, 1 H), 7.29 (d, J = 9.3, 1 H), 7.22, (dd, J = 9.3, 2.4, 1 H), 7.12 (s, 1 H), 7.05 (s, 1 H), 2.31 (d, J = 5.8, 4 H), 1.07-1.01 (m, 2 H), 0.57-0.53 (m, 4 H), 0.26-0.23 (m, 4 H).

EXAMPLE 21

6-(bis-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **223**, Structure 7 of Scheme II, where $R^1 = R^2$ = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroaldehyde sequentially in place of paraformaldehyde alone. Compound **223** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 10.99 (s, 1 H), 7.44 (d, J = 8.9, 1 H), 7.32 (s, 1 H), 7.29 (d, J = 8.9, 1 H), 7.11 (s, 1 H), 4.07 (q, J = 8.4, 4 H).

EXAMPLE 22

6-(bis-2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **224**, Structure 7 of Scheme II, where $R^1 = R^2$ = pentafluoroethylmethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using 2,2,3,3,3-pentafluoropropyraldehyde in place of

paraformaldehyde. Compound **224** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.1 (bs, 1 H), 7.35 (s, 1 H), 7.34 (d, J = 8.8, 1 H), 7.28 (dd, J = 8.8, 2.4, 1 H), 7.10 (s, 1 H), 4.14 (t, J = 16.9, 4 H).

EXAMPLE 23

6-(bis-2-Chloro-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **225**, Structure **7** of Scheme II, where $R^1 = R^2$ = chlorodifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using chlorodifluoroacetic acid in place of difluoroacetic acid. Compound **225** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.12 (bs, 1 H), 7.66 (dd, J = 2.6, 9.1, 1 H), 7.50 (d, J = 9.1, 1 H), 7.46 (s, 1 H), 6.95 (s, 1 H), 4.55 (t, J = 12.1, 4 H).

EXAMPLE 24

6-(bis-2-Bromoethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **226**, Structure **7** of Scheme II, where $R^1 = R^2$ = 2-bromoethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using bromoacetic acid in place of difluoroacetic acid. Compound **226** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$) 11.06(bs, 1H), 7.41 (d, J = 9.0, 1H), 7.12 (d, J = 9.0, 1H), 7.09 (s, 1H), 6.98 (s, 1H), 3.85 (t, J = 7.2, 4H), 3.50 (t, J = 7.2, 4H).

EXAMPLE 25

6-(N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **227**, Structure **7** of Scheme II, where R^1 = H, R^2 = 2,2,2-trichloroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **200** (Structure **3** of Scheme II) and trichloroacetic acid. Compound **227** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$) 10.53 (bs, 1H), 7.40 (d, J = 9.6, 1H), 7.15 (d, J = 9.6, 1H), 7.13 (s, 1H), 7.09 (s, 1H), 4.62 (t, J = 7.2, 1H), 4.19 (d, J = 7.2, 2H).

EXAMPLE 26

6-(bis-N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 228, Structure 7 of Scheme II, where $R^1 = R^2 =$ 2,2,2-trichloroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **200** (Structure **3** of Scheme II) and trichloroacetic acid. Compound **228** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$) 10.82 (bs, 1H), 7.65 (s, 1H), 7.57 (d, J = 8.8, 1H), 7.45 (d, J = 8.8, 1H), 7.10 (s, 1H), 4.70 (s, 4H).

EXAMPLE 27

6-(N-2,2,2-Chlorodifluoroethyl-N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 229, Structure 7 of Scheme II, where R^1 = 2,2,2-chlorodifluoroethyl, R^2 = 2,2,2-trichloroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **200** (Structure **3** of Scheme II) and trichloroacetic acid and chlorodifluoroacetic acid. Compound **229** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$) 10.86(bs, 1H), 7.34 (d, J = 9.0, 1H), 7.21 (dd, J = 9.1, 2.6, 1H), 7.16 (s, 1H), 7.09 (s, 1H), 5.97 (tt, J = 55, 3.8, 1H), 3.83 (td, J = 13.9, 3.9, 4H).

EXAMPLE 28

6-(bis-N-2,2-Difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 230, Structure 7 of Scheme II, where $R^1 = R^2 =$ 2,2-dilfuoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **200** (Structure **3** of Scheme II) and difluoroacetic acid. Compound **230** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$) 11.47 (bs, 1H), 7.34 (d, J = 9.0, 1H), 7.21 (dd, J = 9.1, 2.6, 1H), 7.16 (s, 1H), 7.09 (s, 1H), 5.97 (tt, J = 55, 3.8, 1H), 3.83 (td, J = 13.9, 3.9, 4H).

EXAMPLE 29

6-(N-2,2-Dichloroethyl-N-2,2,2-trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 231, Structure 7 of Scheme II, where R^1 = 2,2,2-trichloroethyl, R^2 = 2,2-dichloroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **200** (Structure **3** of Scheme II) and dichloroacetic acid and trichloroacetic acid. Compound **231** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$) 11.01 (bs, 1H), 7.44 (s, 2H), 7.42 (s, 1H), 7.41(s, 1H), 7.12 (s, 1H), 5.74 (t, *J* = 6.3, 1H), 4.58 (s, 2H), 4.33 (d, *J* = 6.3, 2H).

EXAMPLE 30

6-(bis-N-2,2-Dichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 232, Structure 7 of Scheme II, where R^1 = R^2 = 2,2-dichloroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **200** (Structure **3** of Scheme II) and dichloroacetic acid. Compound **232** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.2 (bs, 1H), 7.51 (s, 2H), 7.19 (s, 1H), 6.94 (s, 1H), 6.25 (t, *J* = 6.3, 2H), 4.29 (d, *J* = 6.3, 4H).

EXAMPLE 31

6-(N-2,2-Dichloroethyl-N-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 233, Structure 7 of Scheme II, where R^1 = 2,2-dichloroethyl, R^2 = 2,2-difluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **200** (Structure **3** of Scheme II) and dichloroacetic acid and difluoroacetic acid. Compound **233** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$): 10.60 (bs, 1H), 7.47 (d, *J* = 9.1, 1H), 7.2 (dd, *J* = 9.1, 2.6, 1H), 7.11 (s, 2H), 5.95 (tt, *J* = 55, 3.8, 1H), 5.87 (t, J-6.2, 1H), 4.1 (d, *J* = 6.2, 2H), 3.94, (td, *J* = 13.9, 3.9, 2H).

EXAMPLE 32

6-(N-2,2-Dichloroethyl-N-2,2,2-chlorodifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 234, Structure 7 of Scheme II, where R^1 = 2,2-dichloroethyl, R^2 = 2,2,2-chlorodifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **200** (Structure **3** of Scheme II) and dichloroacetic acid and chlorodifluoroacetic acid. Compound **234** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$) 11.21 (bs, 1H), 7.43 (d, J = 9.0, 1H), 7.24 (d, J = 9.0, 1H), 7.21(s, 1H), 7.11 (s, 1H), 5.84 (t, J = 6.2, 1H), 4.3 (t, J = 11.5, 2H), 4.15 (d, J = 6.2, 2H).

EXAMPLE 33

6-(N-Isopropyl-N-methyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 235, Structure 7 of Scheme II, where R^1 = methyl, R^2 = isopropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using paraformaldehyde and acetone sequentially in place of paraformaldehyde alone. Compound **235** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 10.9 (bs, 1 H), 7.41 (d, J = 9.3, 1 H), 7.36 (dd, J = 9.3, 2.9, 1 H), 7.00 (bs, 1 H) 6.88 (s, 1 H), 4.16-4.11 (m, 1 H), 2.78 (s, 3 H), 1.19 (d, J = 6.8, 6 H).

EXAMPLE 34

6-(N-Methyl-N-cyclopentyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 236, Structure 7 of Scheme II, where R^1 = cyclopentyl, R^2 = methyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using paraformaldehyde and cyclopentanone sequentially in place of paraformaldehyde alone. Compound **236** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.4 (bs, 1 H), 7.28 (d, J = 8.8, 1 H), 7.25 (dd, J = 8.8, 2.4, 1 H), 7.10 (s, 1 H), 7.06, 1 H), 4.14-4.06 (m, 1 H), 2.84 (s, 3 H), 1.94-1.87 (m, 2 H), 1.78-1.73 (m, 2 H), 1.67-1.59 (m, 4 H).

EXAMPLE 35

6-(N-Methyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 237, Structure 7 of Scheme II, where R^1 = methyl, R^2 = isobutyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using paraformaldehyde and isobutyraldehyde sequentially in place of paraformaldehyde alone. Compound **237** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.0 (bs, 1 H), 7.25 (d, J = 9.3, 1 H), 7.08 (dd, J = 9.3, 2.9, 1 H), 7.04 (s, 1 H), 6.93 (s, 1 H), 3.14 (d, J = 7.3, 2 H), 3.01 (s, 3 H), 2.08-2.03 (m, 1 H), 0.94 (d, J = 6.8, 6 H).

EXAMPLE 36

6-(N-Ethyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 238, Structure 7 of Scheme II, where R^1 = propyl, R^2 = ethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using propyraldehyde and acetaldehyde sequentially in place of paraformaldehyde alone. Compound **238** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 10.7 (bs, 1 H), 7.21 (d, J = 9.3, 1 H), 7.06, (dd, J = 9.3, 2.4, 1 H), 7.03 (s, 1 H), 6.93 (s, 1 H), 3.41 (q, J = 7.3, 2 H), 3.25 (t, J = 7.3, 2 H), 1.66-1.61 (m, 2 H), 1.18 (t, J = 7.3, 3 H), 0.97 (t, J = 7.3, 3 H).

EXAMPLE 37

6-(N-Ethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 239, Structure 7 of Scheme II, where R^1 = isopropyl, R^2 = ethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetaldehyde and acetone sequentially in place of paraformaldehyde alone. Compound **239** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.6 (bs, 1 H), 7.29 (d, J = 8.8, 1 H), 7.17, (dd, J = 8.8, 2.9, 1 H), 7.05 (s, 1 H), 7.03 (s, 1 H), 4.04-3.99 (m, 1 H), 3.28 (q, J = 6.8, 2 H), 1.22 (d, J = 6.8, 6 H), 1.18 (t, J = 6.8, 3 H).

EXAMPLE 38

6-(N-Ethyl-N-1-metylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **240**, Structure 7 of Scheme II, where R^1 = ethyl, R^2 = 1-methylpropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetaldehyde and 2-butanone sequentially in place of paraformaldehyde alone. Compound **240** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.5 (bs, 1 H), 7.27 (d, *J* = 9.3, 1 H), 7.16 (dd, *J* = 9.3, 2.4, 1 H), 7.04 (s, 1 H), 7.02 (s, 1 H), 3.76-3.69 (m, 1 H), 3.33-3.24 (m, 2 H), 1.71-1.62 (m, 1 H), 1.54-1.49 (m, 1 H), 1.19 (d, *J* = 6.8, 3 H), 1.17 (t, *J* = 6.8, 3 H), 0.93 (t, *J* = 7.3, 3 H).

EXAMPLE 39

6-(N-Ethyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **241**, Structure 7 of Scheme II, where R^1 = ethyl, R^2 = isobutyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetaldehyde and isobutyraldehyde sequentially in place of paraformaldehyde alone. Compound **241** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.6 (bs, 1 H), 7.28 (d, *J* = 9.3, 1 H), 7.07 (dd, *J* = 9.3, 2.4, 1 H), 7.04 (s, 1 H), 6.92 (s, 1 H), 3.43 (q, *J* = 6.8, 2 H), 3.08 (d, *J* = 7.3, 2 H), 2.03-2.01 (m, 1 H), 1.15 (t, *J* = 6.8, 3 H), 0.95 (d, *J* = 6.8, 6 H).

EXAMPLE 40

6-(N-Ethyl-N-2,2-dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **242**, Structure 7 of Scheme II, where R^1 = ethyl, R^2 = 2,2-dimethylpropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetaldehyde and trimethylacetaldehyde sequentially in place of paraformaldehyde alone. Compound **242** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.2 (bs, 1 H), 7.23 (d, *J* = 8.8, 1 H), 7.07 (dd, *J* = 8.8, 2.9, 1 H), 7.05 (s, 1 H), 7.03 (s, 1 H), 3.47 (q, *J* = 6.8, 2 H), 3.12 (s, 2 H), 1.11 (t, *J* = 6.8, 3 H), 0.99 (s, 9 H).

EXAMPLE 41

6-(N-Ethyl-N-cyclopentyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 243, Structure 7 of Scheme II, where R^1 = cyclopentyl, R^2 = ethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetaldehyde and cyclopentanone sequentially in place of paraformaldehyde alone. Compound **243** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.6 (bs, 1 H), 7.29 (d, J = 9.3, 1 H), 7.22, (dd, J = 9.3, 2.4, 1 H), 7.12 (s, 1 H), 7.06 (s, 1 H), 3.98-3.93 (m, 1 H), 3.32 (q, J = 7.3, 2 H), 1.98-1.95 (m, 2 H), 1.77-1.73 (m, 2 H), 1.66-1.62 (m, 2 H), 1.59-1 53 (m, 2 H), 1.14 (t, J = 7.3, 3 H).

EXAMPLE 42

6-(N-Ethyl-N-1-acetylethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 244, Structure 7 of Scheme II, where R^1 = ethyl, R^2 = 1-acetylethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetaldehyde and 2,3-butanedione sequentially in place of paraformaldehyde alone. Compound **244** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.6 (bs, 1 H), 7.31 (d, J = 8.8, 1 H), 7.10 (dd, J = 8.8, 2.4, 1 H), 7.07 (s, 1 H), 7.01 (s, 1 H), 4.21 (q, J = 6.8, 1 H), 3.42-3.30 (m, 2 H), 2.18 (s, 3 H), 1.39 (d, J = 6.8, 3 H), 1.22 (t, J = 7.3, 3 H).

EXAMPLE 43

(±)-6-(N-Ethyl-N-1-methyl-2-hydroxypropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 245, Structure 7 of Scheme II, where R^1 = ethyl, R^2 = 1-methyl-2-hydroxypropyl)

This compound was prepared by sodium borohydride reduction of Compound **244** (Structure 7 of Scheme II, where R^1 = ethyl, R^2 = 1-acetylethyl) in methanol. Compound **245** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 10.9 (bs, 1 H), 7.40-7.39 (m, 2 H), 7.12, (s, 1 H), 6.88 (s, 1 H), 3.93-3.82 (m, 1 H), 3.65 (d, J = 2.9, 1 H), 3.61-3.56 (m, 1 H), 3.42-3.37 (m, 2 H), 1.21-1.13 (m, 9 H).

EXAMPLE 44

6-(N-Ethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **246**, Structure 7 of Scheme II, where R^1 = ethyl, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetaldehyde and trifluoroacetaldehyde sequentially in place of paraformaldehyde alone. Compound **246** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.02 (s, 1 H), 7.46 (d, J = 9.1, 1 H), 7.38 (dd, J = 9.1, 2.7, 1 H), 7.10 (s, 1 H), 6.92 (s, 1 H), 4.18 (q, J = 9.3, 2 H), 3.61 (q, J = 7.0, 2 H), 1.22 (t, J = 7.0, 3 H).

EXAMPLE 45

6-(N-Ethyl-N-3-furylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **247**, Structure 7 of Scheme II, where R^1 = ethyl, R^2 = 3-furylmethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetaldehyde and 3-furaldehyde sequentially in place of paraformaldehyde alone. Compound **247** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.3 (bs, 1 H), 7.37 (t, J = 1.0, 1 H), 7.30 (s, 1 H), 7.25 (d, J = 9.3, 1 H), 7.13 (dd, J = 9.3, 2.4, 1 H), 7.04 (s, 2 H), 6.30 (s, 1 H), 4.36 (s, 2 H), 3.46 (q, J = 7.3, 2 H), 1.20 (t, J = 7.3, 3 H).

EXAMPLE 46

(±)-6-(N-Ethyl-N-2,2-dimethoxyisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **248**, Structure 7 of Scheme II, where R^1 = ethyl, R^2 = 2,2-dimethoxyisopropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetaldehyde and α,α-dimethoxyacetone sequentially in place of paraformaldehyde alone. Compound **248** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.4 (bs, 1 H), 7.27 (d, J = 9.3, 1 H), 7.20, (dd, J = 9.3, 2.4, 1 H), 7.08 (s, 1 H), 7.05 (s, 1 H), 4.23 (d, J = 5.4, 1 H), 3.93 (dq, J = 6.8, 5.4, 1 H), 3.43 (s, 3 H), 3.42-3.33 (m, 2 H), 3.35 (s, 3 H), 1.26 (d, J = 6.8, 3 H), 1.17 (t, J = 7.3, 3 H).

EXAMPLE 47

6-(N-Isopropyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 249, Structure 7 of Scheme II, where R^1 = propyl, R^2 = isopropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using propyraldehyde and acetone sequentially in place of paraformaldehyde alone. Compound **249** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 12.1 (bs, 1 H), 7.33 (d, J = 9.3, 1 H), 7.15 (dd, J = 9.3, 2.4, 1 H), 7.05 (s, 1 H), 7.00 (s, 1 H), 4.04-3.99 (m, 1 H), 3.11 (t, J = 6.8, 1 H), 1.60-1.54 (m, 2 H), 1.20 (d, J = 6.3, 6 H), 0.95 (t, J = 7.3, 3 H).

EXAMPLE 48

6-(N-2-Hydroxyethyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 250, Structure 7 of Scheme II, where R^1 = 2-hydroxyethyl, R^2 = propyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using propyraldehyde and glyoxal sequentially in place of paraformaldehyde alone. Compound **250** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 10.8 (bs, 1 H), 7.38 (d, J = 9.3, 1 H), 7.25 (dd, J = 9.3, 2.9, 1 H), 6.93 (s, 1 H), 6.86 (s, 1 H), 3.85 (t, J = 5.8, 1 H), 3.75 (dt, J = 7.8, 5.8, 2 H), 3.53 (t, J = 6.3, 2 H), 3.39 (t, J = 7.8, 2 H), 1.67-1.61 (m, 2 H), 0.95 (t, J = 7.3, 3 H).

EXAMPLE 49

(±)-6-(N-Propyl-N-1-methylbutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 251, Structure 7 of Scheme II, where R^1 = propyl, R^2 = 1-methylbutyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using propyraldehyde and 3-methyl-2-butanone sequentially in place of paraformaldehyde alone. Compound **251** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$), 11.7 (bs, 1 H), 7.29 (d, J = 8.8, 1 H), 7.15 (dd, J = 8.8, 2.5, 1 H), 7.04 (s, 1 H), 6.99 (s, 1 H), 3.84-3.80 (m, 1 H), 3.12-3.09 (m, 2 H), 1.65-1.31 (m, 6 H), 1.17 (d, J = 6.3, 3 H), 0.94 (t, J = 7.3, 3 H), 0.91 (t, J = 7.3, 3 H).

EXAMPLE 50

(±)-6-(N-Propyl-N-1,2-dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 252, Structure 7 of Scheme II, where R^1 = propyl, R^2 = 1,2-dimethylpropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using propyraldehyde and 3-methyl-2-butanone sequentially in place of paraformaldehyde alone. Compound **252** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 10.8 (bs, 1 H), 7.21 (d, *J* = 9.3, 1 H), 7.16, (dd, *J* = 9.3, 2.4, 1 H), 7.03 (s, 1 H), 6.98 (s, 1 H), 3.42-3.39 (m, 1 H), 3.12 (t, *J* = 6.8, 2 H), 1.92-1.86 (m, 1 H), 1.61-1.55 (m, 2 H), 1.19 (d, *J* = 6.3, 3 H), 0.99 (d, *J* = 6.3, 3 H), 0.97 (t, *J* = 7.3, 3 H), 0.91 (d, *J* = 6.3, 3 H).

EXAMPLE 51

6-(N-Propyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 253, Structure 7 of Scheme II, where R^1 = propyl, R^2 = isopropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using propyraldehyde and isobutyraldehyde sequentially in place of paraformaldehyde alone. Compound **253** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.5 (bs, 1 H), 7.26 (d, *J* = 8.8, 1 H), 7.05, (dd, *J* = 8.8, 2.4, 1 H), 7.03 (s, 1 H), 6.90 (s, 1 H), 3.31 (t, *J* = 7.3, 2 H), 3.11 (d, *J* = 7.3, 2 H), 2.05-2.00 (m, 1 H), 1.64-1.58 (m, 2 H), 0.94 (d, *J* = 6.8, 6 H), 0.93 (t, *J* = 7.3, 3 H).

EXAMPLE 52

6-(N-Propyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 254, Structure 7 of Scheme II, where R^1 = propyl, R^2 = cyclopropylmethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using propyraldehyde and cyclopropanecarboxaldehyde sequentially in place of paraformaldehyde alone. Compound **254** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 9.9 (bs, 1 H), 7.15 (d, *J* = 8.8, 1 H), 7.12 (dd, *J* = 8.8, 2.4, 1 H), 7.02 (s, 1 H), 7.00 (s, 1 H), 3.35 (t, *J* = 6.8, 2 H), 3.24 (d, *J* = 6.3, 2 H), 1.66-1.61 (m, 2 H), 1.04-1.01 (m, 1 H), 0.95 (t, *J* = 7.3, 3 H), 0.57-0.55 (m, 2 H), 0.26-0.24 (m, 2 H).

EXAMPLE 53

(±)-6-(N-Propyl-N-1-methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 255, Structure 7 of Scheme II, where R^1 = propyl, R^2 = *sec*-butyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using propyraldehyde and 2-butanone sequentially in place of paraformaldehyde alone. Compound **255** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.2 (bs, 1 H), 7.25 (dd, J = 9.3, 2.4, 1 H), 7.15 (dd, J=9.3, 2.4, 1 H), 7.03 (s, 1 H), 7.00 (s, 1 H), 3.70 (q, J = 6.8, 1 H), 3/12-3.09 (m, 2 H), 1.58-1.47 (m, 2 H), 1.18 (d, J = 6.3, 3 H), 0.93-0.91 (m, 6 H).

EXAMPLE 54

6-(N-2-Hydroxyethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 256, Structure 7 of Scheme II, where R^1 = 2-hydroxyethyl, R^2 = isopropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetone and glyoxal sequentially in place of paraformaldehyde alone. Compound **256** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 10.9 (bs, 1 H), 7.41 (d, J = 8.8, 1 H), 7.37 (dd, J = 8.8, 2.9, 1 H), 7.10 (s, 1 H), 6.88 (s, 1 H), 4.09-4.03 (m, 1 H), 3.83 (t, J = 5.6, 1 H), 3.68 (dt, J = 6.8, 5.6, 2 H), 3.38 (t, J = 6.8, 2 H), 1.23 (d, J = 6.8, 6 H).

EXAMPLE 55

6-(N-Isopropyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 257, Structure 7 of Scheme II, where R^1 = isopropyl, R^2 = cyclopropylmethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using acetone and cyclopropanecarboxaldehyde sequentially in place of paraformaldehyde alone. Compound **257** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.0 (bs, 1 H), 7.19 (s, 2 H), 7.04 (s, 2 H), 4.03-3.98 (m, 1 H), 3.08 (d, J = 5.4, 2 H), 1.21 (d, J = 6.4, 6 H), 0.98-0.93 (m, 1 H), 0.58-0.55 (m, 2 H), 0.26-0.23 (m, 2 H).

EXAMPLE 56

6-(N-Methyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 258, Structure 7 of Scheme II, where R^1 = methyl, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using paraformaldehyde and trifluoroacetaldehyde sequentially. Compound **258** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.3 (bs, 1 H), 7.31 (d, J = 9.3, 1 H), 7.18 (dd, J = 9.3, 2.9, 1 H), 7.11 (s, 1 H), 7.08 (s, 1 H), 3.91 (q, J_{H-F} = 8.8, 2 H), 3.13 (s, 3 H).

EXAMPLE 57

6-(N-2,2,2-trifluoroethyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 259, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = isobutyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and isobutyraldehyde sequentially in place of paraformaldehyde alone. Compound **259** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.31 (s, 1 H), 7.29 (d, J = 9.3, 1 H), 7.23 (d, J = 9.3, 1 H), 7.19 (s, 1 H), 7.06 (s, 1 H), 3.94 (q, J = 8.9, 2 H), 3.25 (d, J = 7.3, 2 H), 2.09-2.03 (m, 1 H), 0.94 (d, J = 6.3, 6 H).

EXAMPLE 58

6-(N-2,2,2-trifluoroethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 260, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = isopropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and isopropyraldehyde sequentially in place of paraformaldehyde alone. Compound **260** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.10 (s, 1 H), 7.45 (d, J = 9.1, 1 H), 7.33 (dd, J = 9.1, 2.6, 1 H), 7.30 (s, 1 H), 7.11 (s, 1 H), 4.07-3.95 (m, 1 H), 3.83 (q, J = 8.8, 2 H), 1.24 (d, J = 6.6, 6 H).

EXAMPLE 59

6-(N-2,2,2-Trifluoroethyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **261**, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = cyclopropylmethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and cyclopropanecarboxaldehyde sequentially in place of paraformaldehyde alone. Compound **261** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 10.83 (s, 1 H), 7.42 (d, J = 9.0, 1 H), 7.27 (dd, J = 9.0, 2.7, 1 H), 7.22 (d, J = 2.7, 1 H), 7.09 (s, 1 H), 4.03 (q, J = 8.8, 2 H), 3.34 (d, J = 6.3, 2 H), 1.09-1.00 (m, 1 H), 0.64-0.59 (m, 2 H), 0.31-0.27 (m, 2 H).

EXAMPLE 60

(±)-6-(N-2,2,2-Trifluoroethyl-N-1-methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **262**, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = *sec*-butyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and 2-butanone sequentially in place of paraformaldehyde alone. Compound **262** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 10.87 (s, 1 H), 7.30-7.23 (m, 3 H), 7.05 (s, 1 H), 3.81 (q, J = 8.6, 2 H), 3.63-3.58 (m, 1 H), 1.21 (d, J = 6.7, 3 H), 1.02-0.86 (m, 5 H).

EXAMPLE 61

(±)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **263**, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 2-chloroisopropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and chloroacetone sequentially. Compound **263** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.99 (s, 1H), 7.43 (s, 2H), 7.13 (s, 1H), 6.90 (s, 1H), 4.35 (q, J = 7.8, 2H), 4.22-4.17 (m, 1H), 3.61 (dd, J = 15.3, 3.6, 1H), 3.42 (dd, J = 15.3, 8.3, 1H), 1.20 (d, J = 6.2, 3H).

EXAMPLE 62

(+)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **264**, Structure **7** of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 2-chloroisopropyl) and (-)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **265**, Structure **7** of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 2-chloroisopropyl)

Compounds **264** and **265** were prepared by chiral HPLC separation of Compound **263**.

EXAMPLE 63

6-(N-2,2,2-Trifluoroethyl-N-3-furfuryl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **266**, Structure **7** of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 3-furanylmethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and 3-furaldehyde sequentially. Compound **266** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.98 (s, 1H), 7.77 (s, 1H), 7.43 (s, 3H), 7.19 (s, 1H), 6.89 (s, 1H), 6.42 (s, 1H), 4.62 (s, 2H), 6.27 (q, J = 9.1, 2H).

EXAMPLE 64

6-(N-2,2,2-Trifluoroethyl-N-3-thiophenemethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **267**, Structure **7** of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 3-thiophenemethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and 3-thiophenecarboxaldehyde sequentially. Compound **267** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.99 (s, 1H), 7.31-7.29 (m, 3H), 7.13 (s, 1H), 7.02 (s, 1H), 6.92 (d, J = 4.6, 1H), 6.76 (s, 1H), 4.66 (s, 2H), 4.21 (q, J = 9.2, 2H).

EXAMPLE 65

6-(N-2,2,2-Trifluoroethyl-N-3,3-dimethylbutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 268, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 3,3-dimethylbutyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and 3,3-dimethylbutyraldehyde sequentially. Compound **268** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.99 (s, 1H), 7.33 (d, J = 9.2, 1H), 7.21 (dd, J = 9.1, 2.6, 1H), 6.97 (s, 1H), 6.79 (s, 1H), 4.06 (q, J = 9.2, 2H), 3.45 (m, 2H), 1.45 (m, 2H), 0.88 (s, 9H).

EXAMPLE 66

6-(N-2,2,2-Trifluoroethyl-N-2-thiophenemethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 269, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 2-thiophenemethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and 2-thiophenecarboxaldehyde sequentially. Compound **269** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.92 (s, 1H), 7.45-7.42 (m, 3H), 7.33 (d, J = 5.4, 1H), 7.24 (s, 1H), 7.08 (s, 1H), 6.96 (t, J = 4.4, 1H), 6.88 (s, 1H), 4.96(s, 2H), 4.31 (q, J = 9.0, 2H).

EXAMPLE 67

6-(N-2,2,2-Trifluoroethyl-N-2-furfuryl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 270, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 2-furanylmethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and 2-furaldehyde sequentially. Compound **270** was isolated as a yellow solid. ^{1}H NMR (400 MHz, acetone-d_6) 10.92 (s, 1H), 7.50 (s, 1H), 7.47-7.42 (m, 2H), 7.25 (s, 1H), 6.89 (s, 1H), 6.37-6.34 (m, 2H), 4.72 (s, 2H), 4.29 (q, J = 9.2, 2H).

EXAMPLE 68

6-(N-Butyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **271**, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = butyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and butyraldehyde sequentially. Compound **271** was isolated as a yellow solid. ^{1}H NMR (400 MHz, acetone-d_6) 11.04 (s, 1H), 7.45 (d, J = 9.1, 1H), 7.37 (dd, J = 9.1, 2.5, 1H), 7.10 (s, 1H), 6.91 (s, 1H), 4.19 (q, J = 9.3, 2H), 3.52 (t, J = 7.7, 2H), 1.9-1.61 (m, 2H), 1.46-1.37 (m, 2H), 0.96 (t, J = 7.4, 3H).

EXAMPLE 69

6-(bis-N,N-Benzyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **272**, Structure 7 of Scheme II, where R^1 = R^2 = benzyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using benzaldehyde. Compound **272** was isolated as a yellow solid. ^{1}H NMR (400 MHz, acetone-d_6) 11.60 (s, 1H), 7.41-7.25 (m, 12H), 6.98 (s, 1H), 6.83 (s, 1H), 4.79 (s, 4H).

EXAMPLE 70

6-(N-2,2,2-Trifluoroethyl-N-cyclobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **273**, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = cyclobutyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and cyclobutanone sequentially in place of paraformaldehyde alone. Compound **293** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 10.85 (s, 1 H), 7.30-7.25 (m, 2 H), 7.16 (s, 1 H), 7.06 (m, 1 H), 4.18-4.08 (m, 1 H), 3.86 (q, J = 8.9, 2 H), 2.40-2.34 (m, 2 H), 1.97-1.92 (m, 2 H), 1.79-1.77 (m, 2 H).

EXAMPLE 71

6-(N-2,2,2-Trifluoroethyl-N-2,2-dichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **274**, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 2,2-dichloroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using trifluoroacetic acid and dichloroacetic acid sequentially in place of

difluoroacetic acid. Compound **274** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.26 (s, 1H), 7.58 (dd, J = 9.2, 2.7, 1H), 7.50 (d, J = 9.1, 1H), 7.32 (s, 1H), 6.97 (s, 1H), 6.26 (t, J = 6.4, 1H), 4.45 (q, J = 9.0, 2H), 4.23 (d, J = 6.4, 2H).

EXAMPLE 72

6-(N-2,2,2-Trifluoroethyl-N-2-chloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 275, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 2-chloroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using trifluoroacetic acid and chloroacetic acid sequentially in place of difluoroacetic acid. Compound **275** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.10 (s, 1H), 7.48 (d, J = 2.5, 2H), 7.17 (s, 1H), 6.93 (s, 1H), 4.34 (q, J = 9.2, 2H), 3.92 (dd, J = 13.9, 7.1, 2H), 3.80 (dd, J = 13.9, 7.1, 2H).

EXAMPLE 73

6-(N-Benzyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 276, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = benzyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and benzaldehyde sequentially in place of paraformaldehyde alone. Compound **276** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.62 (s, 1H), 7.39 (d, J = 2.3, 2H), 7.38-7.31 (m, 4H), 7.27-7.22 (m, 1H), 7.09 (s, 1H), 6.86 (s, 1H), 4.81 (s, 2H), 4.41 (q, J = 9.2, 2H).

EXAMPLE 74

6-(N-4-Fluorobenzyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 277, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = benzyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and 4-fluorobenzaldehyde sequentially in place of paraformaldehyde alone. Compound **277** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.05 (s, 1H), 7.40 (s, 1H), 7.39-7.34 (m, 3H), 7.10-7.06 (m, 3H), 6.86 (s, 1H), 4.80 (s, 2H), 4.41 (q, J = 9.2, 2H).

EXAMPLE 75

6-(N-Propyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **278**, Structure 7 of Scheme II, where R^1 = propyl, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and propyraldehyde sequentially in place of paraformaldehyde alone. Compound **278** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.03 (s, 1 H), 7.45 (d, J = 9.1, 1 H), 7.38 (dd, J = 9.1, 2.3, 1 H), 7.09 (s, 1 H), 6.91 (s, 1 H), 4.24-4.17 (m, 2 H), 3.48 (t, J = 7.6, 2 H).

EXAMPLE 76

6-(N-2,2,3,3,3-Pentafluoropropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2 (1*H*)-quinolinone (Compound **279**, Structure 7 of Scheme II, where R^1 = 2,2,3,3,3-pentafluoropropyl, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and pentafluoropropyraldehyde sequentially in place of paraformaldehyde alone. Compound **279** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.8 (bs, 1 H), 7.39 (d, J = 8.8, 1 H), 7.33 (s, 1 H), 7.29 (dd, J = 8.8, 2.9, 1 H), 7.10 (s, 1 H), 4.13 (t, $J_{H\text{-}F}$ = 15.1, 2 H), 4.08 (q, $J_{H\text{-}F}$ = 8.3, 2 H).

EXAMPLE 77

6-Diallylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **280**, Structure 7 of Scheme II, where R^1 = R^3 = allyl)

This compound was prepared from Compound **200** and allyl bromide by the following General Procedure IX (Allylation of amine):

To a solution of Compound 200 (Structure 3 of Scheme II) in methanol (0.05-0.2 M) was added K_2CO_3 powder (5-10 equiv) and an allyl bromide (3-10 equiv). The reaction mixture was stirred at room temperature for 3 hrs and extracted with EtOAc. The organic layer was washed with H_2O, dried (Na_2SO_4), and concentrated *in vacuo*. Purification by chromatography afforded a white solid in excellent yield (80-95%).

Compound 280 was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.01 (s, 1 H), 7.27 (d, J = 2.6, 1 H), 7.20 (d, J = 9.1, 1 H), 7.07 (dd, J = 9.1, 2.6, 1 H), 7.02 (s, 1 H), 5.90-5.81 (m, 2 H), 3.20 (dd, J = 15.6, 3.9, 4 H), 3.97 (d, J = 3.9, 4 H).

EXAMPLE 78

6-(N-Isobutyl-N-allyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **281**, Structure 7 of Scheme II, where R^1 = isobutyl, R^2 = allyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII to install isobutyl from isobutyraldehyde and sequentially in a similar fashion as that described in Example 77, General Procedure IX to install allyl group from allyl bromide. Compound **281** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.2 (bs, 1 H), 7.23 (d, J = 9.3, 1 H), 7.06 (dd, J = 9.3, 2.4, 1 H), 7.03 (s, 1 H), 6.97 (s, 1 H), 5.85-5.77 (m, 1 H), 5.19-5.12 (m, 2 H), 4.00-3.99 (m, 2 H), 3.15 (d, J = 7.3, 2 H), 2.09-2.03 (m, 1 H), 0.97 (d, J = 6.8, 6 H).

EXAMPLE 79

6-(N-Isopropyl-N-allyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **282**, Structure 7 of Scheme II, where R^1 = isopropyl, R^2 = allyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII to install isopropyl from isopropyraldehyde and sequentially in a similar fashion as that described in Example 77, General Procedure IX to install allyl group from allyl bromide. Compound **282** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 10.8 (bs, 1 H), 7.21 (d, J = 9.3, 1 H), 7.13 (dd, J = 9.3, 2.4, 1 H), 7.06 (s, 1 H), 7.02 (s, 1 H), 5.89-5.82 (m, 1 H), 5.26 (dd, J = 17.1, 1.5, 1 H), 5.18 (dd, J = 10.3, 1.5, 1 H), 4.12-4.07 (m, 1 H), 3.84-3.83 (m, 2 H), 1.22 (d, J = 6.4, 6 H).

EXAMPLE 80

6-(N-Allyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **283**, Structure 7 of Scheme II, where R^1 = allyl, R^2 = 2,2,2-trifluoroethyl)

6-Allylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **284**, Structure **7** of Scheme II, where R^1 = allyl, R^2 = H):

To a solution of Compound **200** (Structure **3** of Scheme II) (340 mg, 1.49 mmol) in MeOH (20 mL) was added K_2CO_3 (1.0 g) followed by allylbromide (0.30 mL, 3.5 mmol). After stirring at room temperature for 6 h, water was added and the mixture was extracted with EtOAc (3x 50 mL). The combined organic layers were washed with brine, and dried over $MgSO_4$, concentrated in vacuo and purified by column chromatography (Silica gel, hex:EtOAc, 3:1 to 1:1 gradient) to give 184 mg of Compound **284**.

6-(N-Allyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **283**, Structure **7** of Scheme II, where R^1 = allyl, R^2 = 2,2,2-trifluoroethyl):

To a solution of Compound **284** (261 mg, 0.97 mmol) in TFA (8 mL) was added trifluoroacetaldehyde hydrate (0.5 mL, 5 mmol) and the mixture was stirred at room temperature for 6 h. $NaCNBH_3$ (60 mg, 1 mmol) was added and the mixture was stirred for 16 h. Then additional $NaCNBH_3$ (60 mg, 1 mmol) was added and the mixture was stirred for 2 h. The reaction was quenched with water (20 mL) and was extracted with EtOAc (2x 40 mL). The combined organic layer was dried over $MgSO_4$, concentrated in vacuo and purified by column chromatography (Silica gel, hex : EtOAc 5 : 2) to give Compound **283** (201 mg, 0.57 mmol) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 2.0 (bs, 1 H), 7.35 (d, J = 9.8, 1 H), 7.19-7.16 (m, 2 H), 7.08 (s, 1 H), 5.87-5.80 (m, 1 H), 5.27 (dd, J = 10.7, 1.5, 1 H), 5.19 (dd, J = 17.6, 1.5, 1 H), 4.10 (d, J = 4.9, 2 H), 3.92 (q, $J_{H\text{-}F}$ = 8.8, 2 H).

EXAMPLE 81

6-(N-Allyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **285**, Structure **7** of Scheme II, where R^1 = allyl, R^2 = cyclopropylmethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII to install cyclopropylmethyl group from cyclopropanecarboxaldehyde and sequentially in a similar fashion as that described in Example 77, General Procedure IX to install allyl group from allyl bromide. Compound **285** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 10.7 (bs, 1 H), 7.38 (d, J = 9.1, 1 H), 7.15 (dd, J = 9.1, 2.5, 1 H), 7.06 (s, 1 H), 7.05 (s, 1 H), 5.90- 5.80 (m, 1 H), 5.20 (d, J = 5.4, 1 H), 5.17 (s, 1 H), 4.04 (d, J = 4.7, 2 H), 3.27 (d, J = 6.2, 2 H), 1.08- 1.03 (m, 1 H), 0.59- 0.55 (m, 2 H), 0.27- 0.23 (m, 2 H).

EXAMPLE 82

6-(N-Allyl-N-2,2,2-trifluoroacetyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **286**, Structure 7 of Scheme II, where R^1 = allyl, R^2 = 2,2,2-trifluoroacetyl)

This compound was prepared in a similar fashion as that described in Example 11, General Procedure VII but using Compound **284** (Structure 7 of Scheme II, where R^1 = H, R^2 = allyl) and trifluoroacetic anhydride in place of Compound **200** and acetic anhydride. Compound **286** was isolated as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) 12.9 (bs, 1 H), 7.69 (s, 1 H), 7.57 (d, *J* = 8.8, 1 H), 7.48 (dd, *J* = 8.8, 2.4, 1 H), 7.17 (s, 1 H), 5.90-5.87 (m, 1 H), 5.26 (d, *J* = 9.8, 1 H), 5.14 (d, *J* = 17.1, 1 H), 4.36 (s, 2 H).

EXAMPLE 83

6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroacetyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **287**, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = trifluoroacetyl)

This compound was prepared in a similar fashion as that described in Example 11, General Procedure VII but using Compound **209** (Structure 7 of Scheme II, where R^1 = H, R^2 = 2,2,2-trifluoroethyl) and trifluoroacetic anhydride in place of Compound **200** and acetic anhydride. Compound **287** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.57 (s, 1 H), 7.78 (s, 1 H) 7.53-7.32 (m, 2 H), 7.17 (s, 1 H), 4.45-4.39 (m, 2 H).

EXAMPLE 84

6-(N-Allyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **288**, Structure 7 of Scheme II, where R^1 = allyl, R^2 = propyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII to install propyl group from propionaldehyde and sequentially in a similar fashion as that described in Example 77, General Procedure IX to install allyl group from allyl bromide. Compound **288** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 10.9 (bs, 1 H), 7.21 (d, *J* = 9.3, 1 H), 7.05 (dd, *J* = 9.3, 2.9, 1 H), 7.03 (s, 1 H), 6.96 (s, 1 H), 5.87-5.80 (m, 1 H), 5.19- 5.16 (m, 2 H), 3.96 (d, *J* = 4.9, 2 H), 3.31 (t, *J* = 7.3, 2 H), 1.67-1.61 (m, 2 H), 0.96 (t, *J* = 7.3, 3 H).

EXAMPLE 85

(±)-6-(N-2-Hydroxyisopropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 289, Structure 7 of Scheme II, where R^1 = 2-hydroxyisopropyl, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and acetol sequentially in place of paraformaldehyde alone. Compound **289** was isolated as a yellow solid: ^1H NMR (500 MHz, $CDCl_3$) 11.6 (bs, 1 H), 7.44 (s, 1 H), 7.41 (dd, J = 8.8, 2.4, 1 H), 7.35 (d, J = 8.8, 1 H), 7.09 (s, 1 H), 3.96- 3.88 (m, 1 H), 3.85- 3.78 (m, 2 H), 3.67- 3.61 (m, 2 H), 2.06 (d, J = 1.4, 1 H), 1.14 (d, J = 6.8, 3 H).

EXAMPLE 86

(±)-6-(N-Isobutyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 290, Structure 7 of Scheme II, where R^1 = isobutyl, R^2 = 2,2,2-trifluoroisopropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetone and 2-butanone sequentially in place of paraformaldehyde alone. Compound **290** was isolated as a yellow solid: ^1H NMR (500 MHz, $CDCl_3$) 12.3 (bs, 1 H), 7.38 (d, J = 8.8, 1 H), 7.30 (dd, J = 8.8, 2.4, 1 H), 7.28 (s, 1 H), 7.09 (s, 1 H), 4.12-4.06 (m, 1 H), 3.05 (d, J = 7.3, 2 H), 1.83-1.78 (m, 1 H) 1.41 (d, J = 6.8, 3 H), 0.89-0.87 (m, 6 H).

EXAMPLE 87

6-(N-2,2-Difluoroethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 291, Structure 7 of Scheme II, where R^1 = 2,2-difluoroethyl, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **211** (Structure 7 of Scheme II, where R^1 = H, R^2 = 2,2-difluoroethyl) and trifluoroacetic acid in place of Compound **200** and difluoroacetic acid. Compound **291** was isolated as a yellow solid: ^1H NMR (400 MHz, acetone-d_6) 11.55 (s, 1 H), 7.54 (dd, J = 9.1, 2.4, 1 H), 7.49 (d, J = 9.1, 1 H), 7.29 (s, 1 H), 6.96 (s, 1 H), 6.21 (tt, J = 55.5, 3.9, 1 H), 4.37 (m, 2 H), 4.02 (td, J = 14.2, 3.9, 2 H).

EXAMPLE 88

6-(N-2,2-Dimethylpropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 292, Structure 7 of Scheme II, where R^1 = 2,2-dimethylpropyl, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **211** (Structure 7 of Scheme II, where R^1 = H, R^2 = 2,2-difluoroethyl) and trimethylacetic acid in place of Compound **200** and difluoroacetic acid. Compound **292** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 12.2 (bs, 1 H), 7.36 (d, J = 9.8, 1 H), 7.33-7.31 (m, 2 H), 7.09 (s, 1 H), 4.03 (q, J_{H-F} = 8.8, 2 H), 3.36 (s, 2 H), 0.94 (s, 9 H).

EXAMPLE 89

6-(N-2,2-Difluoro-2-chloroethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 293, Structure 7 of Scheme II, where R^1 = 2,2-difluoro-2-chloroethyl, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **209** (Structure 7 of Scheme II, where R^1 = H, R^2 = 2,2,2-trifluoroethyl) and chlorodifluoroacetic acid in place of Compound **200** and difluoroacetic acid. Compound **293** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.18 (s, 1 H), 7.64 (dd, J = 9.1, 2.4, 1 H), 7.52 (d, J = 9.1, 1 H), 7.43 (s, 1 H), 6.99 (s, 1 H), 4.52 (t, J = 12.1, 2 H), 4.43 (m, 2 H).

EXAMPLE 90

6-(N-2,2-Difluoro-2-chloroethyl-N-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 294, Structure 7 of Scheme II, where R^1 = 2,2-difluoroethyl, R^2 = 2,2-difluoro-2-chloroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **211** (Structure 7 of Scheme II, where R^1 = H, R^2 = 2,2-difluoroethyl) and chlorodifluoroacetic acid in place of Compound **200** and difluoroacetic acid. Compound **294** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.44 (d, J = 9.2, 1

H), 7.27 (m, 2 H), 7.11 (s, 1 H), 5.97 (tt, $J = 3.9, 55.8$ Hz), 4.20 (t, $J = 11.7$, 2 H), 3.90 (td, $J_d = 3.8$, $J_t = 13.6$, 2 H).

EXAMPLE 91

6-(N-2,2,2-Trifluoroethyl-N-methylsufonyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **295**, Structure 7 of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = methylsulfonyl)

To pyridine (0.3 mL) was added Compound **209** (Structure **7** of Scheme II, where R^1 = H, R^2 = 2,2,2-trifluoroethyl) (10.0 mg, 0.03 mmol) followed by methanesulfonyl chloride (6.8 mg, 0.06 mmol) and the reaction mixture heated at 60 °C for 18 h. The cooled reaction mixture was diluted with EtOAc and with water. The organic layers were dried over $MgSO_4$, concentrated in vacuo, and chromatographed (MeOH:CH_2Cl_2, 1:19) to produce 2.2 mg (19%) Compound **295** as a brown solid: R_f 0.80 (MeOH: CH_2Cl_2, 1:19); ^{1}H NMR (400 MHz, $CDCl_3$) 7.90 (d, $J = 9.1$, 1H), 7.46 (s, 1H), 7.26-7.28 (m, 1H), 7.13 (s, 1H), 3.93 (quin, $J = 7.3$, 2H), 3.60 (s, 3H).

EXAMPLE 92

1-Methyl-6-(N-propyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **296**, Structure 9 of Scheme II, where R^1 = propyl, R^2 = isobutyl, R^3 = methyl)

This compound was prepared from Compound **243** and iodomethane by the following General Procedure X (Methylation of amide):

To a solution of a 2-quinolinone, such as Compound **253** (Structure **7** of Scheme II, where R^1 = propyl, R^2 = isobutyl) in THF (0.05-0.2 M) was added sodium hydride (60% in mineral oil, 1.2-2.0 equivalents) and iodomethane (2-5 equivalents), the resulting mixture was stirred at room temperature for 1 h until the alkylation went completion by TLC. The mixture was quenched with water, extracted with EtOAc, and concentrated. Chromatography of the crude mixture afforded the N-alkylated product in excellent yield (80-95%).

Compound **296** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 7.30 (d, $J = 9.3$, 1 H), 7.07 (dd, $J = 9.3, 2.9$, 1 H), 7.07 (s, 1 H), 6.97 (s, 1 H), 3.71 (s, 3 H), 3.33 (t, $J = 7.3$, 2 H), 3.13 (d, $J = 7.3$, 2 H), 2.07-2.01 (m, 1 H), 1.64-1.59 (m, 2 H), 0.96-0.93 (m, 9 H).

EXAMPLE 93

1-Methyl-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 297, Structure 9 of Scheme II, where $R^1 = R^2$ = 2,2,2-trifluoroethyl, R^3 = methyl)

This compound was prepared in a similar fashion as that described in Example 92, General Procedure X but using Compound **223** (Structure **7** of Scheme II, where $R^1 = R^2$ = 2,2,2-trifluoroethyl) in place of Compound **253**. Compound **297** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.39 (d, J = 9.4, 1 H), 7.36 (s, 1 H), 7.30 (d, J = 9.4, 1 H), 7.12 (s, 1 H), 4.11-4.05 (m, 2 H), 3.73 (s, 3 H).

EXAMPLE 94

1-Ethyl-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 298, Structure 9 of Scheme II, where $R^1 = R^2$ = 2,2,2-trifluoroethyl, R^3 = ethyl)

This compound was prepared in a similar fashion as that described in Example 92, General Procedure X from Compound **223** (Structure **7** of Scheme II, where $R^1 = R^2$ = 2,2,2-trifluoroethyl) and iodoethane. Compound **298** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.41 (d, J = 9.3, 1 H), 7.36 (s, 1 H), 7.30 (dd, J =9.3, 2.9, 1 H), 7.12 (s, 1 H), 4.36 (q, J = 7.3, 2 H), 4.08 (q, J_{H-F} = 8.8, 4 H), 1.37 (t, J = 7.3, 3 H).

EXAMPLE 95

6-(N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound 299, Structure 8 of Scheme II, where R^1 = H, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **209** by the following General Procedure XI (Thioamide formation):

An amide such as Compound **209** (Structure **7** of Scheme II, where R^1 = H, R^2 = 2,2,2-trifluoroethyl) in toluene (0.2-1.0 M) was treated with Lawsson's reagent (1.2 equiv). The reaction mixture was then stirred at room temperature overnight, diluted with EtOAc, washed with sat. $NaHCO_3$, water, brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield crude product. Purification by column chromatography (15-50% EtOAc/hexane) afforded the thioamide in good yield as a yellow solid.

Compound **299** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 10.39 (s, 1 H), 7.66 (d, J = 9.1, 1 H), 7.50 (s, 1 H), 7.36 (dd, J = 9.1, 2.4, 1 H), 7.10 (s, 1 H), 6.20 (s, 1 H), 4.09 (m, 2 H).

EXAMPLE 96

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **300**, Structure **8** of Scheme II, where $R^1 = R^2$ = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **223** (Structure 7 of Scheme II, where $R^1 = R^2$ = 2,2,2-trifluoroethyl) by General Procedure XI described in Example 95. Compound **300** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 12.0 (bs, 1H), 7.74 (s, 1H), 7.48 (d, J = 9.3, 1H), 7.27-7.33 (m, 2H), 4.12 (q, J = 7.8, 4H).

EXAMPLE 97

(±)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **301**, Structure **7** of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 2,2,2-trifluoroisopropyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using trifluoroacetaldehyde and trifluoroacetone sequentially in place of paraformaldehyde alone. Compound **301** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.10 (s, 1 H), 7.68 (d, J = 2.4, 1 H), 7.66 (d, J = 2.4, 1 H), 7.55 (dd, J = 1.7, 21.1, 1 H), 6.96 (s, 1 H), 4.36 (s, 1 H), 4.23 (dq, J = 2.2, 8.8, 2 H), 1.47 (d, J = 7.0, 3 H).

EXAMPLE 98

(+)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **302**, Structure **7** of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 2,2,2-trifluoroisopropyl) and (-)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **303**, Structure **7** of Scheme II, where R^1 = 2,2,2-trifluoroethyl, R^2 = 2,2,2-trifluoroisopropyl)

Compounds **302** and **303** were prepared by chiral HPLC separation of Compound **301**.

EXAMPLE 99

6-Mercapto-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 305, Structure 13 of Scheme II)

6-Methoxythiocarbonylmercapto-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **304**, Structure **12** of Scheme II)

To a mixture of Compound **200** (Structure **3** of Scheme II) in H_2SO_4 was added aqueous $NaNO_2$ at 0 °C and the resulting mixture was stirred for 1h to give 6-diazo-4-trifluoromethyl-2(1*H*)-quinolinone (Structure **11** of Scheme II). To a solution of potassium *O*-ethylxanthate in water at 50 °C was added the above crude mixture and the reaction was stirred for 2h and cooled down to rt. The mixture was extracted with EtOAc, washed with brine and concentrated. Chromatography afforded Compound **304** as a white solid. ^1H NMR (400 MHz, $CDCl_3$) 11.29 (s, 1H), 7.99 (s, 1H), 7.72 (dd, J = 8.6, 1.7, 1H), 7.50 (d, J = 8.6, 1H), 7.14 (s, 1H), 7.03 (s, 1H), 4.63 (q, J = 7.2, 2H), 1.35 (t, J = 7.2, 3H).

6-Mercapto-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **305**, Structure **13** of Scheme II):

To a solution of Compound **304** in THF was added $LiAlH_4$ in THF at 0 °C and the reaction mixture was warmed to rt till the starting material was consumed by TLC. The reaction was quenched with water, neutralized with HCl (3N aqueous), extracted and washed with brine. Removal of solvent and chromatography afforded Compound **305** as white solids. ^1H NMR (400 MHz, $CDCl_3$) 11.02 (s, 1H), 7.73 (s, 1H), 7.54 (d, J = 8.7, 1H), 7.48 (d, J = 8.7, 1H), 7.08 (s, 1H), 3.62 (s, 1H).

EXAMPLE 100

6-(1,1-Dimethyl-2-propynyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **306**, Structure **10** of Scheme II)

In a r.b. flask, a solution of compound **200** (Structure **3** of Scheme II) in THF was treated with Cu(I)Cl (10 mol%) and 2-acetoxy-2-methyl-3-butyne (1.5 equiv). The reaction mixture was heated to reflux for 18h. After cooling to rt, the reaction mixture was filtered through a pad of celite and the celite cake was rinsed with EtOAc. The filtrate was washed with saturated aqueous NH_4Cl solution, H_2O, and brine. Dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (SiO_2, 5% EtOAc in hexane as eluent) to afford compound **306** as a yellow solid. ^1H NMR (500 MHz, $CDCl_3$) 12.9 (bs, 1H), 7.49 (s,

1H), 7.38 (d, J = 8.8, 1H), 7.20 (dd, J = 8.8, 2.4, 1H), 7.08 (s, 1H), 3.81 (bs, 1H), 2.42 (s, 1H), 1.63 (s, 6H).

EXAMPLE 101

6-*tert*-Butylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 307, Structure 7 of Scheme III, where R^1 = H, R^2 = *tert*-butyl)

6-Bromo-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **308**, Structure **16** of Scheme III):

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 4-bromoaniline in place of aniline. Compound **308** was isolated in 40-60% yield as a white solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.60 (s, 1 H), 7.74 (dd, J = 8.8, 1.9, 1 H), 7.48 (d, J = 8.8, 1 H), 6.99 (s, 1 H).

6-Bromo-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **309**, Structure **17** of Scheme III):

This compound was prepared by the following General Procedure XII:

To a solution of Compound **308** (0.40 g, 1.4 mmol) in DMF (7 mL) was added CsF (0.88 g, 5.8 mmol) and 2-iodopropane (0.66 g, 2.7 mmol) and the reaction mixture was stirred at room temperature overnight till the starting material was consumed. The resulting brown suspension was diluted with EtOAc (50 mL), washed with water (3x 50 mL) and brine and concentrated. Chromatography afforded the 2-isopropyloxyquinoline in 50-90% yield.

Compound **309** was isolated as white crystalline needles (0.24 g, 51%): ^{1}H NMR (400 MHz, $CDCl_3$) 8.10 (d, J = 0.9, 1H), 7.74 (s, 2H), 7.19 (s, 1H), 5.57-5.51 (m, 1H), 1.41 (d, J = 6.2, 6H).

6- *tert*-Butylamino-2-isopropyloxy-4-trifluoromethylquinolines (Compound **310**, Structure **18** of Scheme III, where R^1 = H, R^2 = *tert*-butyl):

This compound was prepared by the following General Procedure XIII (Palladium mediated coupling of aryl bromide and alkylamine):

To a schlenk tube containing a solution of a bicyclic aryl bromide, such as Compound **309** in toluene (0.05-0.2 M) was added Cs_2CO_3 (2-3 equiv), $Pd_2(dba)_3$ (1-3 mol %), and (*R*)-BINAP (2.0 mg, 0.003 mmol, 1.5-4.5 mol%) followed by a primary or secondary amine (3-5 equiv). The resulting yellow reaction mixture was heated to 100 °C for 4-48 h, cooled to room

temperature, diluted with Et_2O, filtered, and concentrated *in vacuo*. Chromatography (CH_2Cl_2:hexane or EtOAc:hexane mixtures) of the crude mixture afforded compounds of Structures **18** or **19**.

Compound **310** was isolated as green oils.

6-*tert*-Butylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **307**, Structure 7 of Scheme III, where R^1 = H, R^2 = *tert*-butyl):

This compound was prepared by the following General Procedure XIV (Hydrolysis of 2-alkyloxyquinoline):

To a 50 mL r.b. flask containing a solution of 2-(isopropylether)-6-alkylamino-4-trifluoromethyl quinoline such as Compound **310** (0.1 mmol) in AcOH (0.5 mL) was added conc. HCl (0.2 mL) and the reaction mixture stirred at rt for 30 min and 100 °C for 30 min. The cooled reaction mixture was diluted with CH_2Cl_2 (25 mL) and neutralized by the dropwise addition of sat. $NaHCO_3$ (approx. 25 mL). The organic layers were washed with sat. $NaHCO_3$ (50 mL) and H_2O (50 mL) and the aqueous layers were back extracted with EtOAc (25 mL). The combined organic layers were dried over $MgSO_4$, concentrated *in vacuo*, and purified by flash chromatography (MeOH:CH_2Cl_2, 1:4 or 1:9) to afford compounds of Structures 7 or **14** in Scheme III (25-95%).

Compound **307** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 12.2-12.4 (bs, 1H), 7.30 (d, J = 8.8, 1H), 7.15 (bs, 1H), 7.03-7.06 (m, 2H), 1.37 (s, 9H).

EXAMPLE 102

6-(1-Piperidinyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **311**, Structure **20** of Scheme III, where R^{3-8} = H, X = methylene)

This compound was prepared in a similar fashion as described in Example 101, General Procedures XIII and XIV from Compound **309** and piperidine as a yellow solid: R_f 0.51 (MeOH: CH_2Cl_2, 1:9); ^{1}H NMR (500 MHz, d_6-acetone) 10.92 (bs, 1 H), 7.42-7.45 (m, 2 H), 7.15 (d, J = 2.0, 1 H), 6.89 (s, 1 H), 3.17 (t, J = 5.4, 4 H), 1.73 (quin, J = 5.9, 4 H), 1.56-1.62 (m, 2 H).

EXAMPLE 103

6-(1-Pyrrolidinyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **312**, Structure **20** of Scheme III, where R^{3-8} = H, X = a bond)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using pyrrolidine in place of piperidine. Compound **312** was isolated as a yellow solid: R_f 0.55 (MeOH:CH_2Cl_2, 1:9); ^{1}H NMR (500 MHz, d_6-acetone) 7.41 (d, J = 9.3, 2 H), 7.07 (dd, J = 2.9, 9.3, 1 H), 6.87 (s, 1 H), 3.31-3.34 (m, 4 H), 2.02-2.04 (m, 4 H).

EXAMPLE 104

6-(1-Morpholino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **313**, Structure **20** of Scheme III, where R^{3-8} = H, X = oxygen)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using morpholine in place of piperidine. Compound **313** was isolated as a yellow solid: R_f 0.35 (MeOH: CH_2Cl_2 1:4); ^{1}H NMR (500 MHz, d_6-acetone) 7.46-7.47 (m, 2 H), 7.15-7.16 (m, 1 H), 6.91 (s, 1 H), 3.82-3.84 (m, 4 H), 3.16-3.18 (m, 4 H).

EXAMPLE 105

(±)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **314**, Structure **20** of Scheme III, where R^{4-8} = H, R^3 = methyl, X = methylene)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using 2-methylpiperidine in place of piperidine. Compound **314** was isolated as a yellow solid: R_f 0.75 (MeOH:CH_2Cl_2, 1:4); ^{1}H NMR (500 MHz, $CDCl_3$) 12.57 (bs, 1 H), 7.34-7.41 (m, 2 H), 7.23-7.26 (m, 1 H), 7.08 (s, 1 H), 3.85-3.86 (m, 1 H), 3.15-3.17 (m, 1 H), 3.03 (t, J = 8.8, 1 H), 1.61-1.91 (m, 6 H), 0.99 (d, J = 6.8, 3 H).

EXAMPLE 106

(+)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **315**, Structure **20** of Scheme III, where R^{4-8} = H, R^3 = methyl, X = methylene) and (-)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **316**, Structure **20** of Scheme III, where R^{4-8} = H, R^3 = methyl, X = methylene)

Compounds **315** and **316** were prepared by chiral HPLC separation of Compound **314**. Compound **315**: $[\alpha]_D$ = +23 and Compound **316**: $[\alpha]_D$ = -30.

EXAMPLE 107

6-(N-phenylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **317**, Structure **7** of Scheme III, where R^1= phenyl, R^2 = H)

6-(N-phenylamino)-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **318**, Structure **18** of Scheme III, where R^1= phenyl, R^2 = H):

This compound was prepared in a similar fashion as that described in Example 101, General Procedure XIII from aniline.

6-(N-phenylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **317**, Structure **7** of Scheme III, where R^1= phenyl, R^2 = H):

This compound was prepared in a similar fashion as that described in Example 101, General Procedure XIV from Compound **318**. Compound **317** was isolated as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) 10.83 (s, 1H), 7.47-7.38 (m, 3H), 7.32-7.26 (m, 2H), 7.09-7.04 (m, 3H), 6.98 (t, *J* = 7.3, 1H), 5.86 (s, 1H).

EXAMPLE 108

6-(N-phenyl-N-ethylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **319**, Structure **7** of Scheme III, where R^1= phenyl, R^2 = ethyl)

6-(N-phenyl-N-ethylamino)-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **320**, Structure **18** of Scheme III, where R^1= phenyl, R^2 = ethyl):

A mixture of Compound **318** (Structure **18** of Scheme III, where R^1= phenyl, R^2 = H), iodoethane and NaH in THF was stirred at rt overnight till the starting material was consumed. The reaction was quenched with water, extracted with EtOAc and concentrated. Chromatography afforded Compound **320** as yellow oil.

6-(N-phenyl-N-ethylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **319**, Structure **7** of Scheme III, where R^1= phenyl, R^2 = ethyl):

This compound was prepared in a similar fashion as that described in Example 101, General Procedure XIV from Compound **320**. Compound **319** was isolated as a yellow solid. ^1H NMR (400 MHz, $CDCl_3$) 11.27 (s, 1H), 7.37-7.27 (m, 6H), 7.01-6.99 (m, 3H), 3.82 (q, J = 7.0, 2H), 1.25 (t, J = 7.0, 3H).

EXAMPLE 109

6-(N-phenyl-N-2,2,2-trifluoroethylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **321**, Structure **7** of Scheme III, where R^1= phenyl, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV from Compound **317** and 2,2,2-trifluoroacetaldehyde. Compound **321** was isolated as a yellow solid. ^1H NMR (400 MHz, acetone-d_6) 11.60 (s, 1H), 7.54 (d, J = 8.7, 1H), 7.49-7.44 (m, 2H), 7.34-7.30 (m, 2H), 7.05-7.00 (m, 3H), 6.95 (s, 1H), 4.61 (q, J = 9.1, 2H).

EXAMPLE 110

(±)-6-(3-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **322**, Structure **20** of Scheme III, where R^{3-4} = R^{6-8} = H, R^5 = methyl, X = methylene)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using 3-methylpiperidine in place of piperidine. Compound **322** was isolated as a yellow solid: R_f 0.81 (EtOAc); ^1H NMR (500 MHz, $CDCl_3$) 10.6-10.8 (bs, 1 H), 7.33 (dd, J = 2.9, 9.3, 1 H), 7.15-7.24 (m, 2 H), 7.05 (s, 1 H), 3.51-3.58 (m, 2 H), 2.69 (dt, J = 2.9, 11.7, 1 H), 2.38 (t, J = 10.7, 1 H), 1.71-1.85 (m, 3 H), 1.68-1.71 (m, 1 H), 1.05-1.11 (m, 1 H), 0.99 (d, J = 6.3, 3 H).

EXAMPLE 111

6-(4-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **323**, Structure **20** of Scheme III, where R^{3-8} = H, X = $CHCH_3$)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using 4-methylpiperidine in place of piperidine. Compound **323** was isolated as a yellow solid: R_f 0.51 (MeOH: CH_2Cl_2, 1:4); ^1H NMR (500

MHz d_6-acetone) 7.42-7.45 (m, 2 H), 7.15 (s, 1 H), 6.89 (s, 1 H), 3.66 (d, J = 12.2, 2 H), 2.65-2.74 (m, 2 H), 1.79 (d, J = 11.7, 2 H), 1.50-1.60 (m, 1 H), 1.32-1.38 (m, 2 H), 0.99 (d, J = 6.3, 3 H).

EXAMPLE 112

6-(*cis*-3,5-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **324**, Structure **20** of Scheme III, where $R^{3-4} = R^{7-8}$ = H, R^{5-6} = methyl, X = methylene)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using *cis*-3,5-dimethylpiperidine in place of piperidine. Compound **324** was isolated as a yellow solid: R_f 0.71 (MeOH: CH_2Cl_2, 1:4); ^{1}H NMR (500 MHz, $CDCl_3$) 10.2-10.4 (bs, 1 H), 7.32 (dd, J = 2.4, 9.3, 1 H), 7.14-7.22 (m, 2 H), 7.05 (s, 1 H), 3.55 (d, J = 11.2, 2 H), 2.26 (t, J = 11.2, 2 H), 1.83-1.85 (m, 3 H), 0.97 (d, J = 6.8, 3 H), 0.71-0.74 (m, 1 H).

EXAMPLE 113

6-(2,6-*cis*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **325**, Structure **20** of Scheme III, where R^{4-7} = H, $R^3 = R^8$ = methyl, X = methylene) and (±)-6-(2,6-*trans*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **326**, Structure **20** of Scheme III, where R^{4-7} = H, $R^3 = R^8$ = methyl, X = methylene)

These compounds were prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using 2,6-dimethylpiperidine in place of piperidine. Compounds **325** and **326** were isolated as a 1:1 mixture as a yellow solid: Compound **325**: ^{1}H NMR (500 MHz, $CDCl_3$) 11.80-12.00 (bs, 1H), 7.34 (s, 2H), 7.21 (s, 1H), 7.08 (s, 1H), 3.56-3.64 (m, 2H), 2.75 (dt, J = 2.4, 12.2, 1H), 2.38 (t, J = 10.7, 1H), 1.68-1.85 (m, 2H), 1.35-1.43 (m, 1H), 1.21-1.28 (m, 1H), 0.99 (d, J = 6.4, 6H); Compound **326**: ^{1}H NMR (500 MHz, $CDCl_3$) 11.80-12.00 (bs, 1H), 7.34 (s, 2H), 7.21 (s, 1H), 7.08 (s, 1H), 3.49-3.54 (m, 2H), 2.69 (dt, J = 2.9, 11.7, 1H), 1.68-1.85 (m, 3H), 1.21-1.28 (m, 1H), 1.06-1.11 (m, 1H), 1.01 (d, J = 6.3, 6H);

EXAMPLE 114

(±)-6-(2-Methyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **327**, Structure **20** of Scheme III, where R^{4-8} = H, R^3 = methyl, X = a bond)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using 2-methylpyrrolidine in place of piperidine. Compound **327** was isolated as a yellow solid: R_f 0.68 (MeOH: CH_2Cl_2, 1:4); ^{1}H NMR (500 MHz, $CDCl_3$) 11.6-11.8 (bs, 1 H), 7.31 (d, *J* = 9.3, 1 H), 7.06 (bs, 1 H), 6.99 (dd, *J* = 2.4, 9.3, 1 H), 6.83 (m, 1 H), 3.91-3.94 (m, 1 H), 3.48 (dt, *J* = 2.9, 9.8, 1 H), 3.22 (q, *J* = 7.3, 1 H), 2.10-2.16 (m, 2 H), 2.02-2.10 (m, 1 H), 1.76-1.77 (m, 1 H), 1.21 (d, *J* = 6.3, 3 H).

EXAMPLE 115

6-(2,5-*cis*-Dimethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **328**, Structure **20** of Scheme III, where R^{4-7} = H, R^3 = R^8 = methyl, X = a bond)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using 2,5-dimethylpyrrolidine in place of piperidine. Compound **328** was isolated as a yellow solid: R_f 0.60 (MeOH: CH_2Cl_2, 1:4); ^{1}H NMR (500 MHz, $CDCl_3$) 11.4-11.8 (bs, 1 H), 7.28-7.30 (m, 1 H), 7.05 (bs, 1 H), 7.02 (dd, *J* = 2.4, 9.3, 1 H), 6.86-6.90 (m, 1 H), 3.79-3.82 (m, 2 H), 2.08-2.14 (m, 2 H), 1.75-1.80 (m, 2 H), 1.31 (d, *J* = 6.8, 6 H).

EXAMPLE 116

(±)-6-(2,5-*trans*-Dimethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **329**, Structure **20** of Scheme III, where R^{4-7} = H, R^3 = R^8 = methyl, X = a bond)

Compound **329** was isolated as a miner isomer of Compound **328** as described in Example 115 as a yellow solid: R_f 0.60 (MeOH: CH_2Cl_2, 1:4); ^{1}H NMR (400 MHz, $CDCl_3$) 11.2-11.4 (bs, 1H), 7.32 (d, *J* = 8.9, 1H), 6.90-7.01 (m, 2H), 6.78-6.82 (m, 1H), 3.88-4.06 (m, 2H), 2.26-2.28 (m, 2H), 1.67-1.69 (m, 2H), 1.12 (d, *J* = 6.2, 6H).

EXAMPLE 117

6-(1-Azepano)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **330**, Structure **20** of Scheme III, where R^{3-8} = H, X = ethylene)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using azepane in place of piperidine. Compound **330** was isolated as a yellow solid: R_f 0.52 (MeOH: CH_2Cl_2, 1:9); ^{1}H NMR (500 MHz, $CDCl_3$) 9.80 (bs, 1 H), 7.14 (s, 1 H), 7.07 (dd, J = 2.4, 9.3, 1 H), 7.02 (bs, 1 H), 6.93-6.95 (m, 1 H), 3.51 (t, J = 5.9, 4 H), 1.57-1.82 (m, 4 H), 1.55-1.60 (m, 4 H).

EXAMPLE 118

(±)-6-(2-Hydroxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)--quinolinone (Compound **331**, Structure **20** of Scheme III, where R^{4-8} = H, R^3 = hydroxymethyl, X = methylene)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using 2-(*tert*-butyldimethylsilyloxymethyl)piperidine in place of piperidine. The silyl protection group was removed under the HCl hydrolysis condition. Compound **331** was isolated as a yellow solid: R_f 0.28 (MeOH: CH_2Cl_2, 1:4); ^{1}H NMR (500 MHz, $CDCl_3$) 11.7-11.9 (bs, 1 H), 7.40 (d, J = 2.4, 1 H), 7.32-7.34 (m, 2 H), 7.07 (bs, 1H), 3.78-3.82 (m, 2 H), 3.62-3.66 (m, 1 H), 3.32-3.35 (m, 1 H), 3.15-3.20 (m, 1 H), 1.57-1.84 (m, 6 H).

EXAMPLE 119

6-(2,5-cis-Dimethyl-1-pyrrolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **332**, Structure **20** of Scheme III, where R^{4-7} = H, R^3 = R^8 = methyl, X = a double bond)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV but using 2,5-dimethylpyrroline in place of piperidine. Diastereomerically pure Compound **332** was isolated as a yellow solid: R_f 0.15 (MeOH: CH_2Cl_2, 1:19); ^{1}H NMR (500 MHz, $CDCl_3$) 11.50-11.70 (bs, 1 H), 7.32 (d, J = 9.3, 1 H), 7.07 (s, 1 H), 7.02 (dd, J = 2.4, 9.3, 1 H), 6.91 (bs, 1 H), 5.83 (s, 2 H) 4.50 (q, J = 5.9, 2 H), 1.39 (d, J = 6.3, 6 H).

EXAMPLE 120

(±)-6-(2-Propyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 333, Structure 20 of Scheme III, where R^3 = propyl, R^{4-8} = H, X = CH_2)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 2-propylpiperidine. Compound **333** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 12.20-12.40 (bs, 1H), 7.35 (, d, *J* = 9.3, 1H), 7.31 (dd, *J* = 2.4, 9.3, 1H), 7.16 (s, 1H), 7.07 (s, 1H), 4.74-4.78 (m, 1H), 3.28-3.31 (m, 1H), 3.02-3.07 (m, 1H), 1.51-1.80 (m, 6H), 1.18-1.42 (m, 4H), 0.86 (t, *J* = 7.3, 3H).

EXAMPLE 121

(±)-6-(2-Methoxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 334, Structure 20 of Scheme III, where R^3 = methoxymethyl, R^{4-8} = H, X = CH_2)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 2-methoxymethylpiperidine. Compound **334** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 7.43 (dd, *J* = 2.4, 9.3, 1H), 7.37 (s, 1H), 7.25-7.30 (m, 1H), 7.11 (s, 1H), 3.80-3.82 (m, 2H), 3.74 (s, 3H), 3.64-3.70 (m, 1H), 3.35-3.75 (m, 1H), 3.15-3.21 (m, 1H), 1.60-1.90 (m, 6H).

EXAMPLE 122

(±)-6-(2-Ethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 335, Structure 20 of Scheme III, where R^3 = ethyl, R^{4-8} = H, X = CH_2)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 2-ethylpiperidine. Compound **335** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 11.40-11.60 (bs, 1H), 7.29-7.30 (m, 2H), 7.16-7.18 (m, 1H), 7.05 (s, 1H), 3.61-3.65 (m, 1H), 3.27-3.30 (m, 1H), 3.02-30.7 (m, 1H), 1.42-1.83 (m, 8H), 0.84 (t, *J* = 7.3, 3H).

EXAMPLE 123

6-(1-Cycloheptylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 336, Structure 20 of Scheme III, where R^{3-8} = H, X = -$(CH_2)_3$-)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and cycloheptylamine. Compound **336** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 11.20-11.40 (bs, 1H), 7.27-7.29 (m, 1H), 7.08 (dd, *J* = 2.4,9.3, 1H), 7.05 (s, 1H), 6.93 (s, 1H), 3.47-3.52 (m, 4H), 1.77-1.81 (m, 4H, 1.53-1.62 (m, 4H), 1.32-1.36 (m, 2H).

EXAMPLE 124

(±)-6-(2-Ethoxycarbonyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 337, Structure 20 of Scheme III, where R^3 = ethoxycarbonyl, R^{4-8} = H, X = -CH_2-)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and ethyl pipecolinate. Compound **337** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 12.00-12.10 (bs, 1H), 7.35 (d, *J* = 9.3, 1H), 7.31 (dd, *J* = 2.0, 8.8, 1H), 7.20 (s, 1H), 4.46 (dd, *J* = 3.4, 5.4, 1H), 4.07-4.12 (m, 2H), 3.41-3.44 (m, 2H), 2.21-2.25 (m, 1H), 1.96-2.03 (m, 1H), 1.87-1.91 (m, 1H), 1.63-1.74 (m, 2H), 1.46-1.56 (m, 1H), 1.18 (t, *J* = 7.3, 3H).

EXAMPLE 125

(±)-6-(2-Isopropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 338, Structure 20 of Scheme III, where R^3 = isopropyl, R^{4-8} = H, X = a bond)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 2-isopropylpyrrolidine. Compound **338** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 12.20-12.40 (bs, 1H), 7.35 (d, *J* = 9.3, 1H), 7.07 (s, 1H), 7.02 (dd, *J* = 2.4, 9.3, 1H), 6.87 (s, 1H), 3.69-3.72 (m, 1H), 3.55-3.59 (m, 1H), 3.23 (q, *J* = 7.8, 1H), 2.16-2.19 (m, 1H), 1.92-2.06 (m, 4H), 0.97 (d, *J* = 6.8, 3H), 0.83 (d, *J* = 6.3, 3H).

EXAMPLE 126

(±)-6-(2-Hydroxycarbonyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 339, Structure 20 of Scheme III, where R^3 = carboxylic acid, R^{4-8} = H, X = -CH_2-)

This compound was prepared by hydrolysis of Compound **337** (Structure **20** of Scheme III, where R^3 = ethyl carboxylate, R^{4-8} = H, X = -CH_2-). Compound **339** was isolated as a yellow solid: R_f = 0.23 (90:9:1 CH_2Cl_2: MeOH: NH_4OH).

EXAMPLE 127

6-(3,5-*cis*-Dimethyl-1-piperazino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 340, Structure 20 of Scheme III, where $R^3 = R^4 = R^7 = R^8$ = H, $R^5 = R^6$ = methyl, X = NH)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 1,6-*cis*-piperazine. Compound **340** was isolated as a yellow solid: ^{1}H NMR (d_6-acetone, 500 MHz) 10.90-11.00 (bs, 1H), 7.57 (dd, *J* = 2.4, 8.8, 1H), 7.50 (d, *J* = 8.8, 1H), 7.27 (s, 1H), 6.93 (s, 1H), 3.87 (d, *J* = 13.2, 2H), 3.69-3.76 (bs, 2H), 3.03 (t, *J* = 11.7, 2H), 1.47 (d, *J* = 6.8, 6H).

EXAMPLE 128

(±)-6-(2-Benzyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 341, Structure 20 of Scheme III, where R^3 = benzyl, $R^4 = R^5 = R^6 = R^7 = R^8$ = H, X = a bond)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 2-benzylpyrrolidine. Compound **341** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 10.50-10.60 (bs, 1H), 7.31-7.36 (m, 2H), 7.23-7.25 (m, 4H), 7.08 (s, 1H), 7.05 (dd, *J* = 2.4, 8.8, 1H), 7.01 (s, 1H), 3.98-4.02 (m, 1H), 3.48-3.52 (m, 2H), 3.25 (q, *J* = 7.8, 1H), 3.07 (dd, *J* = 2.9, 13.7, 1H), 2.57 (dd, *J* = 9.8, 13.7, 1H), 1.93-2.01 (m, 3H).

EXAMPLE 129

(±)-6-(5-Methyl-2-oxo-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 342, Structure 20 of Scheme III, where R^3, R^4 = carbonyl, $R^5 = R^6 = R^7$ = H, R^8 = methyl, X = a bond)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 5-methyl-2-pyrrolidinone. Compound **342** was isolated as yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz)

12.00-12.40 (bs, 1H), 7.77 (dd, J = 2.0, 8.8, 1H), 7.73 (s, 1H), 7.48 (d, J = 8.8, 1H), 7.12 (s, 1H), 4.36 (sextet, J = 6.8, 1H), 2.66-2.73 (m, 1H), 2.57-2.64 (m, 1H), 2.42-2.48 (m, 1H), 1.80-1.86 (m, 1H), 1.25 (d, J = 6.3, 3H).

EXAMPLE 130

(±)-6-(2-(2-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **343**, Structure **20** of Scheme III, where $R^3 = R^4 = R^5 = R^6 = R^7 = H$, R^8 = 2-hydroxyethyl, $X = CH_2$)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 2-(2-*tert*-butyldimethylsilyloxyethyl)piperidine. Compound **343** was isolated as yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) 10.80-11.10 (bs, 1H), 7.25-7.32 (m, 2H), 7.20 (s, 1H), 7.06 (s, 1H), 4.00-4.07 (m, 2H), 3.94-3.99 (m, 1H), 3.32 (d, J = 11.9, 1H), 3.04-3.08 (m, 1H), 1.82-1.97 (m, 3H), 1.65-1.76 (m, 5H).

EXAMPLE 131

(±)-6-(3-Hydroxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **344**, Structure **20** of Scheme III, where $R^3 = R^4 = R^6 = R^7 = R^8 = H$, R^5 = hydroxy, X = a bond)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 3-*tert*-butyldimethylsilyloxypyrrolidine. Compound **344** was isolated as yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 7.11 (d, J = 9.3, 1H), 6.07 (dd, J = 2.4, 9.3, 1H), 6.78 (s, 1H), 6.60 (s, 1H), 4.39-4.41 (m, 1H), 3.33-3.38 (m, 2H), 3.17-3.23 (m, 1H), 3.09 (d, J = 10.0, 1H), 1.91-2.03 (m, 1H), 1.89-1.86 (m, 1H).

EXAMPLE 132

(±)-6-(3-Acetyloxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **345**, Structure **20** of Scheme III, where $R^3 = R^4 = R^6 = R^7 = R^8 = H$, R^5 = acetyloxy, X = a bond)

This compound was prepared by acetylation of Compound **131** (Structure **20** of Scheme III, where $R^3 = R^4 = R^6 = R^7 = R^8 = H$, R^5 = hydroxy, X = a bond) and isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 10.00-10.20 (bs, 1H), 7.20-7.21 (m, 1H), 7.05 (s, 1H), 6.95 (dd, J = 2.7, 9.2, 1H), 6.82 (s, 1H), 5.47 (m, 1H), 3.70 (dd, J = 2.7, 11.0, 1H), 3.52 (q, J = 11.0, 1H), 3.45 (dt, J = 3.0, 8.5, 1H), 3.40 (d, J = 11.0, 1H), 2.23-2.34 (m, 2H), 1.26 (s, 3H).

EXAMPLE 133

6-(3(*R*)-Hydroxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **346**, Structure **20** of Scheme III, where $R^{3-5} = R^{7-8} = H$, R^6 = hydroxy, X = a bond)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 3(*R*)-(*tert*-butyldimethylsilyloxy)pyrrolidine. Compound **346** was isolated as a yellow solid: R_f 0.36 (MeOH:CH_2Cl_2, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$) 7.20 (d, *J* = 9.3, 1H), 6.90-7.00 (m, 2H), 6.72 (s, 1H), 4.51-4.56 (m, 1H), 3.45-3.49 (m, 2H), 3.20-3.25 (m, 2H), 1.95-2.12 (m, 2H).

EXAMPLE 134

6-(1-Indolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **347**, Structure **21** of Scheme III, where n = 0, m = 1)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and indoline. Compound **347** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 11.70-11.80 (bs, 1H), 7.58-7.60 (m, 2H), 7.42 (d, *J* = 9.3, 1H), 7.22 (d, *J* = 7.3, 1H), 7.07-7.14 (m, 3H), 6.81 (dt, *J* = 1.0, 7.3, 1H), 4.02 (t, *J* = 8.3, 2H), 3.20 (t, *J* = 8.3, 2H).

EXAMPLE 135

6-(1-Tetrahydroquinolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **348**, Structure **21** of Scheme III, where n = 0, m = 2)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 1,2,3,4-tetrahydroquinoline. Compound **348** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 11.60-11.80 (bs, 1H), 7.61-7.62 (m, 1H), 7.56 (dd, *J* = 2.4, 8.8, 1H), 7.40 (d, *J* = 8.8, 1H), 7.08-7.10 (m, 2H), 6.94-6.97 (m, 1H), 6.75-6.78 (m, 1H), 6.70 (t, *J* = 8.3, 1H), 3.68 (t, *J* = 5.6, 2H), 2.88 (t, *J* = 5.6, 2H), 2.05-2.12 (m, 2H).

EXAMPLE 136

6-(2-Tetrahydroisoquinolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **349**, Structure **21** of Scheme III, where n = m = 1)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 1,2,3,4-tetrahydroisoquinoline. Compound **349** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 10.80-11.0 (bs, 1H), 7.37 (d, *J* = 2.0, 8.8, 1H), 7.20-7.31 (m, 6H), 7.08 (s, 1H), 4.44 (s, 2H), 3.60 (t, *J* = 5.9, 2H), 3.04 (t, *J* = 5.9, 2H).

EXAMPLE 137

(±)-6-(1,3,3-Trimethyl-6-azabicyclo[3.2.1]octanyl-6-)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **350**, Structure **22** of Scheme III)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and 1,3,3-trimethyl-6-azabicyclo[3.2.1]octane. Compound **350** was isolated as a yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 12.40-12.50 (bs, 1H), 7.35 (d, *J* = 9.3, 1H), 7.07 (s, 1H), 6.89 (dd, *J* = 2.4, 9.3, 1H), 6.68 (s, 1H), 4.12 (q, *J* = 6.8, 1H), 3.10 (q, *J* = 8.8, 2H), 1.96-1.98 (m, 1H), 1.83-1.86 (m, 1H), 1.47-1.60 (m, 2H), 1.43 (d, *J* = 10.7, 1H), 1.35 (d, *J* = 13.6, 1H), 1.18 (s, 3H) 0.95 (3H), 0.77 (s, 3H).

EXAMPLE 138

(±)-6-(2-Trifluoromethyl-5-*cis*-methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **351**, Structure **25** of Scheme IV, where R^2 = methyl, R^3 = trifluoromethyl) and (±)-6-(2-Trifluoromethyl-5-*trans*-methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **352**, Structure **25** of Scheme IV, where R^2 = methyl, R^3 = trifluoromethyl)

These compounds were prepared from Compound **200** by the following General Procedure XV (Formation of oxazolidine from amine):

6-(N-1-Hydroxy-2-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **353**, Structure **24** of Scheme IV, where R^2 = methyl):

This compound was prepared in a similar fashion as that described in Example 3, General Procedure V but using 1-hydroxyacetone (Structure **23** of Scheme IV, where R^2 = methyl) in place of acetone.

6-(2-Trifluoromethyl-5-methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compounds **351** and **352**, Structure **25** of Scheme IV, where R^2 = methyl, R^3 = trifluoromethyl):

To a solution of Compound **353** in benzene (0.2-0.5 M) was added trifluoroacetaldehyde monohydrate or ethyl hemiacetal (3-5 equiv) in the presence of p-toluenesulfonic acid (2-10 mol%). The reaction mixture was refluxed for 5-15 h with azeotropic removal of water with a Dean-Stark condenser. The mixture was diluted with EtOAc and washed with 2 M $NaHCO_3$, and condensed. Chromatography afforded the desired products.

Compound **351** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 12.1 (bs, 1 H), 7.42 (d, *J* = 9.3, 1 H), 7.20 (s, 1 H), 7.17 (d, *J* = 9.3, 1 H), 7.11 (s, 1 H), 5.32 (q, $J_{H\text{-}F}$ = 4.9, 1 H), 4.46 (dd, *J* = 8.3, 6.8, 1 H), 4.11- 4.04 (m, 1 H), 3.99 (dd, *J* = 8.3, 8.3, 1 H), 1.42 (d, *J* = 5.9, 3 H).

Compound **352** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 12.1 (bs, 1 H), 7.40 (d, *J* = 9.3, 1 H), 7.17 (d, *J* = 9.3, 1 H), 7.14 (s, 1 H), 7.11 (s, 1 H), 5.55 (q, $J_{H\text{-}F}$ = 4.4, 1 H), 4.46 (dd, *J* = 8.3, 2.4, 1 H), 4.33- 4.30 (m, 1 H), 3.99 (d, *J* = 8.3, 1 H), 1.19 (d, *J* = 6.3, 3 H).

EXAMPLE 139

(±)-6-(2-Trifluoromethyl-5-cis-ethyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **354**, Structure **25** of Scheme IV, where R^2 = ethyl, R^3 = trifluoromethyl) and (±)-6-(2-Trifluoromethyl-5-trans-ethyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **355**, Structure **25** of Scheme IV, where R^2 = ethyl, R^3 = trifluoromethyl)

These compounds were prepared in a similar fashion as that described in Example 138, General Procedure XV but using 1-hydroxy-2-butanone (Structure **23** of Scheme IV, where R^2 = ethyl) in the place of 1-hydroxyacetone.

Compound **354** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 12.7 (bs, 1 H), 7.46 (d, *J* =8.8, 1 H), 7.20 (s, 1 H), 7.18 (d, *J* = 8.8, 1 H), 7.11 (s, 1 H), 5.31 (q, $J_{H\text{-}F}$ = 4.9, 1 H), 4.44 (dd, *J* = 7.8, 7.2, 1 H), 4.06 (dd, *J* = 7.8, 7.4, 1 H), 3.86-3.82 (m, 1 H), 2.04-1.96 (m, 1 H), 1.66-1.59 (m, 1 H), 0.99 (t, *J* = 7.3, 3 H).

Compound **355** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 12.0 (bs, 1 H), 7.38 (d, J = 8.8, 1 H), 7.15 (d, J = 8.8, 1 H), 7.12 (s, 1 H), 7.10 (s, 1 H), 5.56 (q, $J_{H\text{-}F}$ = 4.4, 1 H), 4.42 (dd, J = 7.3, 6.8, 1 H), 4.13- 4.09 (m, 2 H), 1.74–1.66 (m, 1 H), 1.52- 1.43 (m, 1 H), 0.86 (t, J = 7.3, 3 H).

EXAMPLE 140

(±)-6-(5-Methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **356**, Structure **25** of Scheme IV, where R^2 = methyl, R^3 = H)

These compounds were prepared in a similar fashion as that described in Example 138, General Procedure XV but using formaldehyde in the place of trifluoroacetaldehyde. Compound **356** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 11.9 (bs, 1 H), 7.36 (d, J = 8.8, 1 H), 7.09 (s, 1 H), 6.91 (dd, J = 8.8, 2.4, 1 H), 6.81 (s, 1 H), 5.05 (d, J = 2.4, 1 H), 4.84 (d, J = 2.4, 1 H), 4.19 (dd, J = 8.3, 3.4, 1 H), 3.96-3.93 (m, 1 H), 3.85 (dd, J = 8.3, 3.4, 1 H), 1.31 (d, J = 5.9, 3 H).

EXAMPLE 141

6-(2,5-Dimethyl-1-pyrrolyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **357**, Structure **20** of Scheme IV, where R^3 = R^8 = methyl, R^4, R^5 = a bond, R^7, R^8 = a bond, X = a bond)

To PhH (2.5 mL) and AcOH (0.7 mL) was added Compound **200** (Structure **3** of Scheme IV) (23 mg, 0.10 mmol) and acetonylacetone (Structure **28** of Scheme IV, where R^2 = R^3 = methyl, X = a bond) (14 mg, 0.12 mmol) and the reaction mixture refluxed for 4.5 h while removing water with a Dean-Stark trap. The cooled reaction mixture was diluted with EtOAc and washed successively with 2M HCl, satd. $NaHCO_3$, and brine. The organic layers were dried over $MgSO_4$, concentrated *in vacuo*, and chromatographed twice (MeOH:CH_2Cl_2, 1:9, then gradient of CH_2Cl_2 to MeOH:CH_2Cl_2, 1:9) to produce 18.0 mg (58%) of Compound **357** as a yellow solid: R_f 0.20 (MeOH: CH_2Cl_2, 1:9); ^{1}H NMR (500 MHz, $CDCl_3$) 11.00-11.20 (bs, 1H), 7.73 (s, 1H), 7.46-7.48 (m, 2H), 7.16 (s, 1H), 5.96 (s, 2H), 2.06 (s, 6H).

EXAMPLE 142

6-(N-2,2,2-Trifluoroethyl-N-3,3,3-trifluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 358, Structure 7 of Scheme IV, where R^2 = 2,2,2-trifluoroethyl, R^1 = 3,3,3-trifluoropropyl)

6-Amino-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **359**, Structure **26** of Scheme IV):

This compound was prepared from Compound **200** (Structure **3** of Scheme IV) in a similar fashion as that described in Example 101, General Procedure XII.

6-(N-3,3,3-Trifluoropropyl)amino-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **360**, Structure **26** of Scheme IV):

A mixture of Compound **359**, 3,3,3-trifluoro-1-iodopropane and K_2CO_3 in DMF was heated at 100 °C for 2h and was quenched with water. Extraction with EtOAc, washing with brine and removal of solvent followed by chromatography afforded Compound **360** as yellow oil.

6-(N-2,2,2-Trifluoroethyl-N-3,3,3-trifluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **358**, Structure **7** of Scheme IV, where R^2 = 2,2,2-trifluoroethyl, R^3 = 3,3,3-trifluoropropyl):

This compound was prepared from Compound **360** by reductive alkylation and acidic hydrolysis in similar fashion as that described in Example 2, General Procedure IV and Example 101, General Procedure XIV. Compound **358** was isolated as yellow solid. ^{1}H NMR (400 MHz, acetone-d_6) 10.90 (s, 1H), 7.50 (d, J = 9.2, 1H), 7.43 (dd, J = 9.2, 2.5, 1H), 7.16 (s, 1H), 6.93 (s, 1H), 4.28 (q, J = 9.2, 2H), 3.88-3.84 (m, 2H), 2.75-2.60 (m, 2H).

EXAMPLE 143

6-bis-N,N-Thiomethoxymethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 361, Structure 7 of Scheme IV, where R^1 = R^2 = thiomethoxymethyl) and 6-bis-N,N-Thiomethoxymethylamino-4-trifluoromethyl-2-thiomethoxymethyloxyquinoline (Compound 362, Structure 27 of Scheme IV)

To a solution of Compound **200** (Structure **3** of Scheme IV) in THF was added NaH and chloromethyl methyl sulfide and the reaction mixture was stirred at rt for 1h and quenched with

water. Extraction with EtOAc, washing with brine, removal of solvent and chromatography afforded Compounds **361** and **362**.

Compound **361** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 7.36-7.38 (m, 3H), 7.08 (s, 1H), 5.40 –5.50 (bs, 2H), 4.67 (s, 4H), 2.29 (s, 3H), 2.17 (s, 6H).

Compound **362** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.80-12.00 (bs, 1H), 7.32-7.36 (m, 3H), 7.09 (s, 1H), 4.67 (s, 4H), 2.16 (t, J = 20.5, 6H).

EXAMPLE 144

(±)-6-(2,5-*trans*-Diethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **363**, Structure **20** of Scheme IV, where $R^2 = R^8$ = ethyl, $R^4 = R^5 = R^6 = R^7$ = H, X = a bond) and 6-(2,5-*cis*-Diethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **364**, Structure **20** of Scheme IV, where $R^2 = R^8$ = ethyl, $R^4 = R^5 = R^6 = R^7$ = H, X = a bond)

These compounds were prepared by the following General Procedure XVI:

To a mixture of Compound **200** (Structure **3** of Scheme IV), acetic acid (10% equiv) and KOH (25% equiv) in methanol was added a diketone (2-5 equiv) and a reducing agent such as $Na(CN)BH_3$. The mixture was stirred at elevated temperature till the products were formed by TLC and quenched with water. Removal of solvent and chromatography of the crude residue afforded the pyrrolidinyl compounds in moderate yield.

Compound **363** was isolated as a major product: ^{1}H NMR (500 MHz, $CDCl_3$) 7.23 (d, J = 8.5, 1H), 6.99 (s, 1H), 6.91 (dd, J = 8.5, 2.5, 1H), 6.74 (s, 1H), 3.69 (t, J = 7.5, 2H), 1.73-1.70 (m, 2H), 1.81 (d, J = 5.0, 1H), 1.73-1.69 (m, 2H), 1.18-1.15 (m, 2H), 0.91 (t, J = 7.5, 6H).

Compound **364** was isolated as a minor product: ^{1}H NMR (500 MHz, $CDCl_3$) 7.20 (d, J = 9.0, 1H), 6.99 (s, 1H), 6.97 (dd, J = 9.0, 2.4, 1H), 6.84 (m, 1H), 3.54 (m, 2H), 2.08-2.00 (m, 2H), 1.90-1.78 (m, 4H), 1.42-1.33 (m, 2H), 0.97 (t, J = 7.5, 6H).

EXAMPLE 145

(±)-6-(2,5-*trans*-Dipropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 365, Structure 20 of Scheme IV, where $R^3 = R^8$ = propyl, $R^4 = R^5 = R^6 = R^7$ = H, X = a bond), 6-(2,5-*cis*-Dipropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 366, Structure 20 of Scheme IV, where $R^3 = R^8$ = propyl, $R^4 = R^5 = R^6 = R^7$ = H, X = a bond) and 6-(2,5-Dipropyl-1-pyrrolo)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 367, Structure 20 of Scheme IV, where $R^3 = R^8$ = propyl, , R^4, $R^5 = R^6$, R^7 = X = a bond)

These compounds were prepared from Compound **200** (Structure **3** of Scheme IV) and 4,7-decanedione by General Procedure XVI described in Example **144**.

Compound **365** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.20-11.30 (bs, 1H), 7.23-7.31 (m, 1H), 7.04 (s, 1H), 6.92 (dd, J = 2.4, 8.8, 1H), 6.76 (s, 1H), 3.77 (t, J = 7.8, 2H), 2.09-2.14 (m, 2H), 1.80-1.84 (m, 2H), 1.61-1.68 (m, 2H), 1.26-1.57 (m, 4H), 0.99-1.17 (m, 2H), 0.95 (t, J = 7.3, 6H).

Compound **366** was isolated as yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) 10.60-10.70 (bs, 1H), 7.22 (d, J = 9.3, 1H), 7.03 (s, 1H), 6.97 (dd, J = 2.9, 9.3, 1H), 6.86 (s, 1H), 3.60-3.68 (m, 2H), 2.00-2.18 (m, 2H), 1.77-1.83 (m, 4H), 1.31-1.47 (m, 6H), 1.00 (t, J = 7.3, 6H).

Compound **367** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 12.60-12.80 (bs, 1H), 7.75 (s, 1H), 7.61 (d, J = 8.3, 1H), 7.51 (dd, J = 2.4, 8.8, 1H), 7.19 (s, 1H), 6.00 (s, 2H), 2.30 (t, J = 7.3, 4H), 1.51 (sextet, J = 7.8, 4H), 0.85 (t, J = 7.3, 6H).

EXAMPLE 146

(±)-6-(2,5-*trans*-Dibutyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 369, Structure 20 of Scheme IV, where $R^3 = R^8$ = butyl, $R^4 = R^5 = R^6 = R^7$ = H, X = a bond) and 6-(2,5-*cis*-Dibutyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 368, Structure 20 of Scheme IV, where $R^3 = R^8$ = butyl, $R^4 = R^5 = R^6 = R^7$ = H, X = a bond)

These compounds were prepared from Compound **200** (Structure **3** of Scheme IV) and 5,8-dodecanedione by General Procedure XVI described in Example **144**.

Compound **369** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 9.80-10.00 (bs, 1H), 7.15 (d, J = 8.8, 1H), 7.06 (s, 1H), 6.89 (dd, J = 2.4, 9.3, 1H), 6.75 (s, 1H), 3.73-3.75 (m, 2H), 2.04-2.13 (m, 2H), 1.80-1.88 (m, 2H), 1.60-1.69 (m, 2H), 1.26-1.48 (m, 8H), 0.89-0.94 (m, 6H).

Compound **368** was isolated as yellow oil: ^{1}H NMR ($CDCl_3$, 500 MHz) 9.40-9.60 (bs, 1H), 7.12 (d, J = 8.8, 1H), 7.01 (s, 1H), 6.94-6.95 (m, 1H), 6.85 (s, 1H), 3.56-3.64 (m, 2H), 2.00-2.05 (m, 2H), 1.81-1.90 (m, 4H), 1.26-1.48 (m, 10H), 0.95 (t, J = 6.3, 6H).

EXAMPLE 147

(±)-6-(2,6-*trans*-Diethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **371**, Structure **20** of Scheme IV, where $R^3 = R^8$ = ethyl, $R^4 = R^5 = R^6 = R^7$ = H, X = CH_2) and 6-(2,6-*cis*- Diethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **370**, Structure **20** of Scheme IV, where $R^3 = R^8$ = ethyl, $R^4 = R^5 = R^6 = R^7$ = H, X = CH_2)

These compounds were prepared from Compound **200** (Structure **3** of Scheme IV) and 3,7-nonanedione by General Procedure XVI described in Example **144**.

Compound **371** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.40-11.60 (bs, 1H), 7.27-7.31 (m, 3H), 7.06 (s, 1H), 3.24-3.26 (m, 2H), 1.85-1.89 (m, 2H), 1.50-1.59 (m, 4H), 1.48-1.50 (m, 2H), 1.38-1.48 (m, 2H), 0.77 (t, J = 7.3, 6H).

Compound **370** was isolated as yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 11.20-11.40 (bs, 1H), 7.31-7.36 (m, 3H), 7.06 (s, 1H), 3.09-3.12 (m, 2H), 1.77-1.81 (m, 2H), 1.49-1.53 (m, 2H), 1.23-1.39 (m, 6H), 0.82 (t, J = 7.3, 6H).

EXAMPLE 148

(±)-6-(2,6-*trans*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **373**, Structure **20** of Scheme IV, where $R^3 = R^8$ = methyl, $R^4 = R^5 = R^6 = R^7$ = H, X = CH_2) and 6-(2,6-*cis*- Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **372**, Structure **20** of Scheme IV, where $R^3 = R^8$ = methyl, $R^4 = R^5 = R^6 = R^7$ = H, X = CH_2)

These compounds were prepared from Compound **200** (Structure **3** of Scheme IV) and 2,6-heptanedione by General Procedure XVI described in Example **144**.

Compound **373** was isolated as yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) 11.88 (bs, 1H), 7.38-7.36 (m, 3H), 7.08 (s, 1H), 3.52 (q, J = 6.3, 2H), 1.97-1.90 (m, 2H), 1.68-1.51 (m, 4H), 0.93 (d, J = 5.9, 6H).

Compound **372** was isolated as yellow solid: ^{1}H NMR ($CDCl_3$, 500 MHz) 12.00-12.20 (bs, 1H), 7.58 (bs, 1H), 7.47 (dd, J = 2.0, 8.8, 1H), 7.42 ((dd, J = 1.0, 8.8, 1H), 7.10 (s, 1H),

2.91-2.96 (m, 2H), 1.76-1.84 (m, 3H), 1.52-1.57 (m, 1H), 1.41-1.48 (m, 2H), 0.77 (d, $J = 6.3$, 6H).

EXAMPLE 149

6-(N-Propyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound 374, Structure 31 of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4 = H$, R^5 = propyl, R^6 = 2,2,2-trifluoroethyl)

6-Amino-4-methyl-2(1*H*)-quinolinone (Compound **375**, Structure **30** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4 = H$)

This compound was prepared in a similar fashion as that described in Example 1, General Procedures II and III but using 4-methyl-2(1*H*)-quinolinone (Compound **376**, Structure **29** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4 = H$) in place of Compound **202**. Compound **375** was isolated as a solid: R_f 0.26 (MeOH: CH_2Cl_2, 1:9); ^1H NMR (500 MHz, CD_3OD) 7.19 (d, $J = 8.8$, 1H), 7.08 (d, $J = 2.4$, 1H), 7.04 (dd, $J = 2.4, 8.8$, 1H), 6.47 (s, 1H), 2.47 (s, 3H).

6-(N-Propyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **374**, Structure **31** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4 = H$, R^5 = propyl, R^6 = 2,2,2-trifluoroethyl):

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI to install trifluoroethyl by using trifluoroacetic acid and Example 2, General Procedure IV to install the propyl. Compound **374** was isolated as a solid: R_f 0.53 (MeOH: CH_2Cl_2, 1:19); ^1H NMR (500 MHz, $CDCl_3$) 10.20-10.30 (bs, 1H), 7.18 (d, $J = 8.9$, 1H), 7.00-7.07 (m, 1H), 6.97 (dd, $J = 2.4, 9.3$, 1H), 6.55 (s, 1H), 3.89 (q, $J = 8.9$, 2H), 3.39 (t, $J = 7.8$, 2H), 2.46 (s, 3H), 1.64-1.67 (m, 2H), 0.96 (t, $J = 7.4$, 3H).

EXAMPLE 150

6-(bis-2,2,2-Trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound 377, Structure 31 of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using Compound **375** (Structure **30** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4 = H$) in place of Compound **200**. Compound **377** was isolated as a yellow

solid: R_f 0.40 (MeOH: CH_2Cl_2, 1:9); ^{1}H NMR (500 MHz, $CDCl_3$) 10.80-11.00 (bs, 1H), 7.16-7.25 (m, 3H), 6.56 (bs, 1H), 4.06 (q, J = 8.5, 4H), 2.45 (s, 3H).

EXAMPLE 151

6-(2,5-Dimethyl-1-pyrrolo)-4-methyl-2(1*H*)-quinolinone (Compound 378, Structure 20a of Scheme V, R^4, R^5 = R^6, R^7 = a bond, R^3 = R^8 = methyl, X = a bond), (±)-6-(2,5-*trans*-dimethyl-1-pyrrolidino)-4-methyl-2(1*H*)-quinolinone (Compound 379, Structure 20a of Scheme V, R^3 = R^8 = methyl, R^4 = R^5 = R^6 = R^7 = H, X = a bond) and 6-(2,5-*cis*-dimethyl-1-pyrrolidino)-4-methyl-2(1*H*)-quinolinone (Compound 380, Structure 20a of Scheme V, R^3 = R^8 = methyl, R^4 = R^5 = R^6 = R^7 = H, X = a bond)

These compounds were prepared in a similar fashion as that described in Example 144, General Procedure XVI but using Compound **375** (Structure **30** of Scheme V, where R = methyl, R^1 = R^2 = R^3 = R^4 = H) in place of Compound **200**.

Compound **378** was isolated as a yellow solid: R_f 0.52 (MeOH: CH_2Cl_2, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$) 10.60-10.80 (bs, 1H), 7.54 (s, 1H), 7.37 (s, 2H), 6.63 (s, 1H), 5.94 (s, 2H), 2.48 (s, 3H), 2.04 (s, 6H).

Compound **379** was isolated as yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) 11.15 (bs, 1H), 7.22 (d, J = 8.9, 1H), 6.90 (dd, J = 8.9, 2.5, 1H), 6.68 (d, J = 2.5, 1H), 6.54 (s, 1H), 4.06 (t, J = 6.3, 2H), 2.45 (s, 3H), 2.27 (m, 2H), 1.67 (m, 2H), 1.13 (s, 3H), 1.11 (s, 3H).

Compound **380** was isolated as yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) 10.48 (bs, 1H), 7.17 (d, J = 8.9, 1H), 6.93 (dd, J = 8.9, 2.5, 1H), 6.74 (d, J = 2.5, 1H), 6.53 (s, 1H), 3.78 (m, 2H), 2.46 (s, 3H), 2.09 (m, 2H), 1.76 (m, 2H), 1.32 (s, 3H), 1.31 (s, 3H).

EXAMPLE 152

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound 381, Structure 31 of Scheme V, where R = methyl, R^1 = R^2 = R^3 = R^4 = H, R^5 = isobutyl, R^6 = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **375** (Structure **30** of Scheme V, where R = methyl, R^1 = R^2 = R^3 = R^4 = H) in a similar fashion as that described in Example 9, General Procedure VI to install trifluoroethyl from trifluoroacetic acid and Example 2, General Procedure IV to install the isobutyl. Compound **381** was isolated as a solid: R_f 0.18 (MeOH: CH_2Cl_2, 3:7);

^{1}H NMR (500 MHz, $CDCl_3$) 11.80-12.00 (bs, 1H), 7.32 (d, J = 9.3, 1H), 7.12 (dd, J = 2.4, 9.3, 1H), 7.02 (d, J = 2.9, 1H), 6.56 (s, 1H), 3.92 (q, J = 8.8, 2H), 3.23 (d, J = 7.3, 2H), 2.47 (s, 3H), 2.04 (quin, J = 6.8, 1H), 0.95 (d, J = 6.8, 6H).

EXAMPLE 153

6-(N-2,2,2-Chlorodifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone
(Compound **382**, Structure **31** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4 = R^5$ = H, R^6 = 2,2,2-chlorodifluoroethyl)

This compound was prepared from Compound **375** (Structure **30** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4$ = H) and chlorodifluoroacetic acid in a similar fashion as that described in Example 9, General Procedure VI. Compound **382** was isolated as a solid: ^{1}H NMR ($CDCl_3$) 10.28(bs, 1H), 7.15 (d, J = 8.6, 1H), 7.10 (d, J = 8.6, 1H), 6.91 (s, 1H), 6.54 (s, 1H), 4.13 (t, J = 7.2, 1H), 3.95 (m, 2H), 2.45 (s, 3H).

EXAMPLE 154

6-(bis-N,N-2,2,2-Chlorodifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone
(Compound **383**, Structure **31** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4$ = H, $R^5 = R^6$ = 2,2,2-chlorodifluoroethyl)

This compound was prepared from Compound **375** (Structure **30** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4$ = H) and chlorodifluoroacetic acid in a similar fashion as that described in Example 9, General Procedure VI. Compound **383** was isolated as a solid: ^{1}H NMR ($CDCl_3$) 11.50 (bs, 1H), 7.35 (d, J = 9.7, 1H), 7.25-7.23 (m, 2H), 6.59 (s, 1H), 4.24 (t, J = 12.0, 4H), 2.49 (s, 3H).

EXAMPLE 155

6-(N-2,2,2-Chlorodifluoroethyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone
(Compound **384**, Structure **31** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4$ = H, R^5 = 2,2,2-trifluoroethyl, R^6 = 2,2,2-chlorodifluoroethyl)

This compound was prepared from Compound **375** (Structure **30** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4$ = H) in a similar fashion as that described in Example 9, General Procedure VI using chlorodifluoroacetic acid and trifluoroacetic acid sequentially. Compound

384 was isolated as a solid: ^{1}H NMR ($CDCl_3$) 11.33 (bs, 1H), 7.37 (d, J = 8.5, 1H), 7.23 (d, J = 8.5, 1H), 7.20 (s, 1H), 4.20 (t, J = 11.7, 2H), 4.09 (q, J = 8.5, 2H), 2.48 (s, 3H).

EXAMPLE 156

6-N-Ethylamino-4-methyl-2(1*H*)-quinolinone (Compound **385**, Structure **31** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4 = R^5$ = H, R^6 = ethyl)

This compound was prepared from Compound **375** (Structure **30** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4$ = H) in a similar fashion as that described in Example 9, General Procedure VI using acetic acid. Compound **385** was isolated as a solid: ^{1}H NMR ($CDCl_3$) 11.05 (bs, 1H), 7.23 (d, J = 8.7, 1H), 6.87 (dd, J = 8.7, 2.6, 1H), 6.75 (s, 1H), 6.54 (s, 1H), 3.65 (bs, 1H), 3.21(q, J = 7.1, 2H), 2.45 (s, 3H), 1.30 (t, J = 7.1, 3H).

EXAMPLE 157

6-(N-Ethyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **386**, Structure **31** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4$ = H, R^5 = 2,2,2-trifluoroethyl, R^6 = ethyl)

This compound was prepared from Compound **375** (Structure **30** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4$ = H) in a similar fashion as that described in Example 9, General Procedure VI using acetic acid and trifluoroacetic acid sequentially. Compound **386** was isolated as a solid: ^{1}H NMR ($CDCl_3$) 11.23 (bs, 1H), 7.36 (d, J = 8.9, 1H), 7.08 (dd, J = 9.0, 2.5, 1H), 6.98 (d, J = 2.5, 1H), 6.58 (s, 1H), 3.87 (q, J = 9.0, 2H), 3.52 (q, J = 7.0, 2H), 2.48 (s, 3H), 1.22 (t, J = 7.0, 3H).

EXAMPLE 158

6-N,N-Diethylamino-4-methyl-2(1*H*)-quinolinone (Compound **387**, Structure **31** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4$ = H, $R^5 = R^6$ = ethyl)

This compound was prepared from Compound **375** (Structure **30** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4$ = H) and acetic acid in a similar fashion as that described in Example 9, General Procedure VI. Compound **387** was isolated as a solid: ^{1}H NMR ($CDCl_3$) 11.72 (bs, 1H), 7.29 (d, J = 8.9, 1H), 7.02 (dd, J = 11.6, 2.6, 1H), 6.83 (d, J = 2.6, 1H), 6.55 (s, 1H), 3.38 (q, J = 7.0, 4H), 2.47 (s, 3H), 1.17 (t, J = 7.0, 6H).

EXAMPLE 159

6-(bis-2,2,2-trifluoroethyl)amino-4-ethyl-2(1*H*)-quinolinone (Compound 388, Structure 31 of Scheme V, where R = ethyl, $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = 2,2,2-trifluoroethyl)

6-Amino-4-ethyl-2(1*H*)-quinolinone (Compound **389**, Structure **30** of Scheme V, where R = ethyl, $R^1 = R^2 = R^3 = R^4 = H$):

This compound was prepared in a similar fashion as that described in Example 1, General Procedures II and III but using 4-ethyl-2(1*H*)-quinolinone (Compound **390**, Structure **29** of Scheme V, where R = ethyl, $R^1 = R^2 = R^3 = R^4 = H$) in place of Compound **202**. Compound **389** was isolated as a solid: R_f 0.42 (MeOH: CH_2Cl_2, 1:9); ^1H NMR (500 MHz, CD_3OD) 7.20 (d, J = 8.8, 1H), 7.13 (d, J = 2.4, 1H), 7.04 (dd, J = 2.4, 8.8, 1H), 6.47 (s, 1H), 2.88 (q, J = 7.3, 2H), 1.34 (t, J = 7.3, 3H).

6-(bis-2,2,2-trifluoroethyl)amino-4-ethyl-2(1*H*)-quinolinone (Compound **388**, Structure **31** of Scheme V, where R = ethyl, $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = 2,2,2-trifluoroethyl):

This compound was prepared from Compound **389** in a similar fashion as that described in Example 9, General Procedure VI to install trifluoroethyl from trifluoroacetic acid. Compound **388** was isolated as a solid: R_f 0.53 (MeOH: CH_2Cl_2, 1:9); ^1H NMR (500 MHz, $CDCl_3$) 12.20-12.40 (bs, 1H), 7.41 (d, J = 9.3, 1H), 7.25 (d, J = 2.4, 1H), 7.20 (dd, J = 2.4, 9.3, 1H), 6.62 (s, 1H), 4.05 (q, J = 8.8, 4H), 2.85 (q, J = 7.3, 2H) 1.35 (t, J = 7.3, 3H).

EXAMPLE 160

6-(bis-2,2,2-trifluoroethyl)amino-4-isopropyl-2(1*H*)-quinolinone (Compound 391, Structure 31 of Scheme V, where R = isopropyl, $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = 2,2,2-trifluoroethyl)

6-Amino-4-isopropyl-2(1*H*)-quinolinone (Compound **392**, Structure **30** of Scheme V, where R = isopropyl, $R^1 = R^2 = R^3 = R^4 = H$):

This compound was prepared in a similar fashion as that described in Example 1, General Procedures II and III but using 4-isopropyl-2(1*H*)-quinolinone (Structure **29** of Scheme V, where R = isopropyl, $R^1 = R^2 = R^3 = R^4 = H$) in place of Compound **202**.

6-(bis-2,2,2-trifluoroethyl)amino-4-isopropyl-2(1*H*)-quinolinone (Compound **391**, Structure **31** of Scheme V, where R = isopropyl, $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = 2,2,2-trifluoroethyl):

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **391** and trifluoroacetic acid as a yellow solid. ^{1}H NMR ($CDCl_3$) 11.22 (bs, 1H), 7.42 (d, J = 8.9, 1H), 7.27 (s, 1H), 7.18 (dd, J = 8.9, 2.3, 1H), 6.65 (s, 1H), 4.04 (q, J = 8.5, 4H), 3.30 (quin, J = 6.7, 1H), 1.29 (d, J = 6.7, 6H).

EXAMPLE 161

7-Fluoro-6-(bis-N,N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **393**, Structure **31** of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^4$ = H, R^3 = fluoro, $R^5 = R^6$ = 2,2,2-trifluoroethyl)

7-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **394**, Structure **29** of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^4$ = H, R^3 = fluoro)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 3-fluoroaniline in place of aniline. Compound **394** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.30 (s, 1H), 7.87-7.85 (m, 1H), 7.27 (dd, J = 2.5, 9.8, 1H), 7.16 (dt, J = 2.5, 8.9, 1H), 6.92 (s, 1H).

5-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **395**, Structure **29** of Scheme V, where R = trifluoromethyl, $R^1 = R^3 = R^4$ = H, R^2 = fluoro)

This compound was isolated as a by-product: ^{1}H NMR (400 MHz, acetone-d_6) 11.32 (s, 1H), 7.70-7.65 (m, 1H), 7.38 (d, J = 8.5, 1H), 7.12-7.07 (m, 1H), 7.04 (s, 1H).

6-Amino-7-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **396**, Structure **30** of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^4$ = H, R^3 = fluoro):

This compound was prepared in a similar fashion as that described in Example 1, General Procedures II and III but using Compound **394** in place of Compound **202**. Compound **396** was isolated as a yellow solid.

7-Fluoro-6-(bis-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **393**, Structure **31** of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^4$ = H, R^3 = fluoro, R^5 = R^6 = 2,2,2-trifluoroethyl):

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI to install trifluoroethyl from trifluoroacetic acid but using Compound **396** in place of Compound **200**. Compound **393** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.28 (s, 1H), 7.79 (d, J = 8.2, 1H), 7.34 (d, J = 12.0, 1H), 6.94 (s, 1H), 4.45 (q, J = 8.7, 4H).

EXAMPLE 162

8-Fluoro-6-(bis-N,N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 397, Structure 31 of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^3 = H$, R^4 = fluoro, $R^5 = R^6$ = 2,2,2-trifluoroethyl)

8-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **398**, Structure **29** of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^3 = H$, R^4 = fluoro)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 2-fluoroaniline in place of aniline. Compound **398** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.04 (s, 1H), 7.62 (d, J = 8.7, 1H), 7.535-7.50 (m, 1H), 7.37-7.32 (m, 1H), 7.02 (s, 1H).

6-Amino-8-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **399**, Structure **30** of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^3 = H$, R^4 = fluoro):

This compound was prepared in a similar fashion as that described in Example 1, General Procedures II and III but using Compound **398** in place of Compound **202**. Compound **399** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.25 (s, 1H), 6.97 (dd, J = 2.2, 12.6, 1H), 6.96 (s, 1H), 6.87-6.86 (m, 1H), 5.16 (s, 2H).

8-Fluoro-6-(N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **400**, Structure **31** of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^3 = R^6 = H$, R^4 = fluoro, R^5 = 2,2,2-trifluoroethyl):

This compound was prepared in a similar fashion as those described in Example 9, General Procedure VI but using Compound **399** in place of Compound **200**. Compound **400** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.88 (s, 1H), 7.15 (dd, J = 12.9, 2.2, 1H), 6.97 (s, 1H), 6.95 (d, J = 9.9, 1H), 6.07 (s, 1H), 4.09-4.02 (m, 2H).

8-Fluoro-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **397**, Structure **31** of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^3 = H$, R^4 = fluoro, $R^5 = R^6$ = 2,2,2-trifluoroethyl):

This compound was prepared in a similar fashion as those described in Example 9, General Procedure VI but using Compound **399** in place of Compound **200** and excess of $NaBH_4$. Compound **397** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.07 (s, 1H), 7.54 (dd, J = 2.5, 13.5, 1H), 7.17 (s, 1H), 7.03 (s, 1H), 4.45 (q, J = 8.7, 4H).

EXAMPLE 163

8-Fluoro-6-(N-2,2,2-trifluoroethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 401, Structure 31 of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^3 = H$, R^4 = fluoro, R^5 = 2,2,2-trifluoroethyl, R^6 = isopropyl)

This compound was prepared in a similar fashion as those described in Example 15, General Procedure VIII but using Compound **400** and acetone in place of Compound **200**. Compound **401** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.50 (s, 1H), 7.46 (d, J = 2.5, 1H), 7.09 (s, 1H), 7.00 (s, 1H), 4.09 (q, J = 8.5, 2H), 2.09-2.02 (m, 1H), 1.26 (d, J = 7.0, 6H).

EXAMPLE 164

6-Amino-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 402, Structure 30 of Scheme V, where R = trifluoromethyl, $R^2 = R^3 = R^4 = H$, R^1 = fluoro)

This compound was prepared in a similar fashion as that described in Example 1, General Procedures I, II and III but using ethyl 2,4,4,4-tetrafluoroacetoacetate in place of ethyl 4,4,4-trifluoroacetoacetate. Compound **402** was isolated as a yellow solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.48 (s, 1H), 7.16 (d, J = 8.7, 1H), 6.92 (dd, J = 2.2, 8.8, 1H), 6.89 (d, J = 2.2, 1H), 5.36 (bs, 1H).

EXAMPLE 165

3-Fluoro-6-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 403, Structure 31 of Scheme V, where R = trifluoromethyl, $R^2 = R^3 = R^4 = R^6 = H$, R^1 = fluoro, R^5 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **402** (Structure **30** of Scheme V, where R = trifluoromethyl, $R^2 = R^3 = R^4 = H$, R^1 = fluoro) and TFA in place of Compound **200** and difluoroacetic acid. Compound **403** was isolated as a yellow solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.55 (s, 1H), 7.26 (d, J = 9.1, 1H), 7.15 (dd, J = 2.1, 9.1, 1H), 6.98 (d, J = 2.1, 1H), 6.54 (t, J = 6.8, 1H), 3.95 (m, 2H).

EXAMPLE 166

3-Fluoro-6-(bis-2,2,2-trifluorofluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 404, Structure 22 of Scheme V, where R = trifluoromethyl, $R^2 = R^3 = R^4 = H$, R^1 = fluoro, $R^5 = R^6$ = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **402** (Structure **30** of Scheme V, where R = trifluoromethyl, $R^2 = R^3 = R^4 = H$, R^1 = fluoro) and TFA in place of Compound **200** and difluoroacetic acid. Compound **404** was isolated as a yellow solid: ^1H NMR (400 MHz, DMSO-d_6) 12.67(s, 1H), 7.53 (dd, J = 2.1, 7.2, 1H), 7.36 (d, J = 9.2, 1H), 7.18 (d, J = 2.1, 1H), 4.39 (q, J = 8.8, 4H).

EXAMPLE 167

6-(bis-Isobutylamino)-4-methyl-2(1*H*)-quinolinone (Compound 405, Structure 31 of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = isobutyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **375** (Structure **30** of Scheme V, where R = methyl, $R^1 = R^2 = R^3 = R^4 = H$) and isobutyric acid. Compound **405** was isolated as a yellow solid: ^1H NMR ($CDCl_3$, 500 MHz) 10.00-10.20 (bs, 1H), 7.12 (d, J = 8.9, 1H), 6.98 (dd, J = 2.4, 8.9, 1H), 6.78 (d, J = 2.4, 1H), 6.52 (s, 1H), 3.17 (d, J = 7.0, 4H), 2.44 (s, 3H), 2.07 (sextet, J = 7.0, 2H), 0.93 (d, J = 6.7, 12H).

EXAMPLE 168

3-Fluoro-6-(N-methyl-N-2,2,2-trifluorofluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 406, Structure 31 of Scheme V, where R = trifluoromethyl, $R^2 = R^3 = R^4 = H$, R^1 = fluoro, R^5 = 2,2,2-trifluoroethyl, R^6 = methyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **403** (Structure **31** of Scheme V, where R = trifluoromethyl, $R^2 = R^3 = R^4 = R^6 = H$, R^1 = fluoro, R^5 = 2,2,2-trifluoroethyl) and parafomaldehyde in place of Compound **200** and propionaldehyde. Compound **406** was isolated as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) 12.25 (bs, 1H), 7.41 (d, J = 8.7, 1H), 7.14 (dd, J = 2.2, 8.8, 1H), 7.13 (d, J = 2.1, 1H), 3.91 (q, J = 8.8, 2H), 3.13 (s, 3H).

EXAMPLE 169

7-Bromo-6-isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 407, Structure 31 of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^4 = R^6 = H$, R^3 = bromo, R^5 = isopropyl)

6-Amino-7-bromo-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **408**, Structure **30** of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^4 = H$, R^3 = bromo):

To a solution of Compound **200** (Structure **3** of Scheme V) in methylene chloride (0.1-0.5 M) was added NBS (1.1 equiv) and the reaction mixture was stirred at room temperature for 30 min. The mixture was concentrated and chromatography afforded Compound **408** as a yellow solid.

7-Bromo-6-isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **407**, Structure **31** of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^4 = R^6 = H$, R^3 = bromo, R^5 = isopropyl):

This compound was prepared in a similar fashion as that described in Example 3, General Procedure V but using Compound **408** in place of Compound **200**. Compound **407** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.3 (bs, 1 H), 7.56 (s, 1 H), 7.07 (s, 1 H), 6.89 (s, 1 H), 4.20 (d, *J* = 5.8, 1 H), 3.70-3.65 (m, 1 H), 1.30 (d, *J* = 6.3, 6 H).

EXAMPLE 170

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-hydroxy-2(1*H*)-quinolinone (Compound 409, Structure 31 of Scheme V, where R = hydroxy, $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 6-amino-4-hydroxy-2(1*H*)-quinolinone (Compound **410**, Structure **30** of Scheme V, where R = hydroxy, $R^1 = R^2 = R^3 = R^4 = H$) and trifluororacetic acid. Compound **409** was isolated as a yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 7.55 (d, *J* = 2.9, 1H), 7.40 (dd, *J* = 2.9, 9.3, 1H), 7.31 (d, *J* = 9.3, 1H), 5.91 (s, 1H), 4.23 (q, *J* = 8.3, 4H).

EXAMPLE 171

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-methoxy-2(1*H*)-quinolinone (Compound 411, Structure 31 of Scheme V, where R = methoxy, $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 6-amino-4-methoxy-2(1*H*)-quinolinone (Compound **412**, Structure **30** of

Scheme V, where R = methoxy, $R^1 = R^2 = R^3 = R^4 = H$) and trifluororacetic acid. Compound **411** was isolated as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) 10.52 (bs, 1H), 7.44, (d, J = 2.7, 1H), 7.29 (d, J = 8.8, 1H), 7.18 (dd, J = 8.8, 2.7, 1H), 6.01 (s, 1H), 4.06 (q, J = 8.53, 4H), 3.99 (s, 3H).

EXAMPLE 172

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-difluoromethyl-2(1*H*)-quinolinone (Compound **413**, Structure **31** of Scheme V, where R = difluoromethyl, $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 6-amino-4-difluoromethyl-2(1*H*)-quinolinone (Compound **414**, Structure **30** of Scheme V, where R = difluoromethyl, $R^1 = R^2 = R^3 = R^4 = H$) and trifluororacetic acid. Compound **413** was isolated as a yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 7.47 (dd, J = 2.9, 9.3, 1H), 7.45 (m, 1H), 7.39 (d, J = 9.3, 1H), 7.15 (t, J = 53.7, 1H), 6.86 (s, 1H), 4.26 (q, J = 8.8, 4H).

EXAMPLE 173

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **415**, Structure **31** of Scheme V, where $R = R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 6-amino-2(1*H*)-quinolinone (Compound **416**, Structure **30** of Scheme V, where $R = R^1 = R^2 = R^3 = R^4 = H$) and trifluororacetic acid. Compound **415** was isolated as a yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 7.92 (d, J = 9.8, 1H), 7.40 (dd, J = 2.9, 8.8, 1H), 7.35 (d, J = 2.9, 1H), 7.32 (d, J = 8.8, 1H), 6.61 (d, J = 9.8, 1H), 4.25 (q, J = 8.8, 4H).

EXAMPLE 174

4-Chloro-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **417**, Structure **31** of Scheme V, where R = chloro, $R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 6-amino-4-chloro-2(1*H*)-quinolinone (Compound **418**, Structure **30** of Scheme V, where R = chloro, $R^1 = R^2 = R^3 = R^4 = H$) and trifluororacetic acid. Compound **417** was isolated as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) 10.30 (bs, 1H), 7.47 (d, J = 2.4, 1H), 7.32 (d, J = 9.3, 1H), 7.25 (dd, J = 9.3, 2.4, 1H), 6.89 (s, 1H), 4.10 (q, J = 8.3, 4H).

EXAMPLE 175

7-Methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **419**, Structure **29** of Scheme V, where R = trifluoromethyl, $R^1 = R^2 = R^4 = H$, R^3 = methoxy)

In a 50-mL flask, a solution of *meta*-anisidine (5 mL, 44 mmol) and ethyl 4,4,4-trifluoroacetoacetate (7.8 mL, 53 mmol, 1.2 equiv) in toluene (5 mL) was heated to reflux for 16 h, cooled and the white precipitate filtered off and washed with hexane (10 mL). The crude precipitate was then heated in EtOH (15 mL) with a catalytic amount of *p*-toluenesulfonic acid. After complete conversion, 4-6 h, the solvent was removed and the crude reaction mixture was re-dissolved in EtOAc (200 mL) and washed with water (2x 20 mL), Brine (20 mL), dried ($MgSO_4$), filtered and concentrated to give 4.0 g (37%) of Compound **419** as a white solid: ^1H NMR (400 MHz, DMSO-d_6) 12.18 (s, 1 H), 7.62 (dd, J = 8.4, 1.5, 1 H), 6.95 (dd, J = 8.2, 2.2, 1 H), 6.93 (s, 1 H), 6.78 (s, 1 H), 3.84 (s, 3 H).

EXAMPLE 176

5,7-Dimethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **420**, Structure **29** of Scheme V, where R = trifluoromethyl, $R^1 = R^4 = H$, $R^2 = R^3$ = methoxy)

This compound was prepared in a similar fashion as that described in Example 175 but using 3,5-dimethoxyaniline in place of 3-anisidine. Compound **420** was isolated as a white solid: ^1H NMR (400 MHz, DMSO-d_6) 12.11 (bs, 1H), 6.71 (s, 1H), 6.56 (d, J = 2.2, 1H), 6.46 (d, J = 2.2, 1H), 3.87 (s, 3H), 3.83 (s, 3H).

EXAMPLE 177

(*R*)-6-(2-Hydroxymethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **421**, Structure **33** of Scheme Va, where n = 1)

(*R*)-6-(2-Methoxycarbonyl-1-pyrrolidino)-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **422**, Structure **32** of Scheme VI, where R = methyl, n = 1)

This compound was prepared in a similar fashion as that described in Example 101, General Procedures XIII and XIV from Compound **309** (Structure **17** of Scheme III) and D-proline methyl ester.

(*R*)-6-(2-Hydroxymethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **421**, Structure **33** of Scheme VI, where n = 1)

This compound was prepared from Compound **422** by a metal hydride reduction and isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.00-11.20 (bs, 1H), 7.26-7.27 (m, 1H), 7.12 (dd, J = 2.7, 9.5, 1H), 7.06 (s, 1H), 6.96 (s, 1H), 3.91-4.14 (m, 1H), 3.71 (s, 2H), 3.58 (t, J = 7.3, 1H), 3.19-3.24 (m, 1H), 2.05-2.16 (m, 5H).

EXAMPLE 178

(*R*)-6-(2-Methoxymethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 423, Structure 34 of Scheme VI, where R = methoxymethyl, n = 1)

This compound was prepared by methylation of Compound **421** and isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.60-11.80 (bs, 1H), 7.32 (d, J = 8.9, 1H), 7.08 (dd, , J = 2.4, 8.9, 1H), 7.07 (s, 1H), 6.96 (s, 1H), 3.92-3.97 (m, 1H), 3.44-3.54 (m, 2H), 3.40 (s, 3H), 3.30 (dd, , J = 7.9, 9.5, 1H), 3.16-3.21 (m, 1H), 2.01-2.13 (m, 4H).

EXAMPLE 179

(±)-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 424, Structure 34 of Scheme VI, where R = chloromethyl, n = 2)

This compound was prepared from Compound **331** (Structure **33** of Scheme VI, where n = 2) by tosylation and chloride displacement. Compound **424** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.60-11.70 (bs, 1H), 7.35 (bs, 2H), 7.25 (s, 1H), 7.08 (s, 1H), 3.96-4.00 (m, 1H), 3.62 (t, J = 10.7, 1H), 3.44-3.47 (m, 1H), 3.29-3.33 (m, 1H), 3.01-3.06 (m, 1H), 2.08-2.18 (m, 1H), 1.82-1.91 (m, 2H), 1.61-1.74 (m, 3H).

EXAMPLE 180

(±)-6-(2-Cyanothiomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 425, Structure 34 of Scheme VI, where R = CH_2SCN, n = 2)

This compound was prepared from Compound **331** (Structure **33** of Scheme VI, where n = 2) by tosylation and thiocyanate displacement. Compound **425** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 12.00-12.20 (bs, 1H), 7.39-7.42 (m, 2H), 7.29 (s, 1H), 7.10 (s, 1H), 4.02 (sextet, J = 4.4, 1H), 3.25-3.27 (m, 1H), 3.16 (dd, J = 4.9, 12.7, 1H), 3.05-3.10 (m, 2H), 1.96-2.05 (m, 2H), 1.68-1.80 (m, 4H).

EXAMPLE 181

(±)-6-(2-Thiomethoxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 426, Structure 34 of Scheme VI, where R = -CH_2SMe, n = 2)

This compound was prepared from Compound **331** (Structure **33** of Scheme VI, where n = 2) by tosylation and methanethiol displacement. Compound **426** was isolated as yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.80-12.00 (bs, 1H), 7.32-7.36 (m, 2H), 7.23 (s, 1H), 7.08 (s, 1H), 3.92-3.95 (m, 1H), 3.28-3.31 (m, 1H), , 3.00-3.05 (m, 1H), 2.72 (dd, *J* = 9.8, 13.2, 1H), 2.45 (dd, *J* = 3.4, 13.2, 1H), 2.04-2.08 (m, 1H), 2.03 (s, 3H), 1.81-1.90 (m, 2H), 1.60-1.70 (m, 3H).

EXAMPLE 182

(±)-6-(2-Cyanomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 427, Structure 34 of Scheme VI, where R = cyanomethyl, n = 2)

This compound was prepared from Compound **331** (Structure **33** of Scheme VI, where n = 2) by tosylation and cyanide displacement. Compound **427** was isolated as red solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 12.20-12.40 (bs, 1H), 7.51-7.54 (m, 4H), 4.11-4.15 (m, 1H), 3.25-3.29 (m, 1H), 3.00-3.04 (m, 1H), 2.59 (dd, *J* = 8.8, 17.1, 1H), 2.40 (dd, *J* = 4.9, 17.1, 1H), 1.84-2.03 (m, 2H), 1.60-1.80 (m, 4H).

EXAMPLE 183

(±)-6-(2-Bromomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 428, Structure 34 of Scheme VI, where R = bromomethyl, n = 2)

This compound was prepared from Compound **331** (Structure **33** of Scheme VI, where n = 2) by tosylation and bromide displacement. Compound **428** was isolated as red solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.40-11.60 (bs, 1H), 7.34-7.35 (m, 2H), 7.25 (s, 1H), 7.08 (s, 1H), 4.00-4.03 (m, 1H), 3.50 (t, *J* = 9.8, 1H), 3.27-3.34 (m, 2H), 3.02-3.06 (m, 1H), 2.15-2.18 (m, 1H), 1.83-1.92 (m, 2H), 1.61-1.73 (m, 3H).

EXAMPLE 184

(±)-6-(2-Iodomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 429, Structure 34 of Scheme VI, where R = iodomethyl, n = 2)

This compound was prepared from Compound **331** (Structure **33** of Scheme VI, where n = 2) by tosylation and iodide displacement. Compound **429** was isolated as red solid. ^{1}H NMR

($CDCl_3$, 500 MHz) 11.80-12.00 (bs, 1H), 7.38 (m, 2H), 7.29-7.26 (m, 1H), 7.08 (s, 1H), 3.80-4.00 (m, 1H), 3.22-3.37 (m, 2H), 3.12-3.20 (m, 1H), 3.01-3.10 (m, 1H), 1.65-1.66 (m, 2H). 1.24-1.30 (m, 4H).

EXAMPLE 185

(+)*R*-6-(2-Iodomethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **430**, Structure **34** of Scheme VI, where R = iodomethyl, n = 1)

This compound was prepared in a similar fashion as that described in Examples 101 and 184 from Compound **309** (Structure **17** of Scheme III) and D-proline and isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 12.5 (bs, 1H), 7.41 (d, J = 8.9, 1H), 7.09 (s, 1H), 6.96 (dd, J = 8.9, 2.4, 1H), 6.83 (s, 1H), 4.09-4.07 (m, 1H), 3.60-3.56 (m, 1H), 3.33-3.30 (m, 1H), 3.27-3.24 (m, 1H), 3.01 (t, J = 10.4, 1H), 2.19-2.05 (m, 4H).

EXAMPLE 186

(±)-6-(2-Fluoromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **431**, Structure **34** of Scheme VI, where R = fluoromethyl, n = 2)

This compound was prepared from Compound **331** (Structure **33** of Scheme VI, where n = 2) by tosylation and fluoride displacement. Compound **431** was isolated as red solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.73 (bs, 1H), 7.32 (d, J = 6.9, 1H), 7.21-7.19 (m, 1H), 7.06-7.04 (m, 2H), 4.95-4.82 (m, 1H), 3.83-3.75 (m, 2H), 3.61-3.40 (m, 2H), 2.01-1.70 (m, 6H).

EXAMPLE 187

(+)S-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **432**, Structure **34** of Scheme VI, where R = chloromethyl, n = 2) and (-)R-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **433**, Structure **34** of Scheme VI, where R = chloromethyl, n = 2)

These compounds were prepared from separation of Compound **424** by chiral HPLC and the absolute sterochemistry were established by independent synthesis from optically active commercial material. Compound **432**: $[\alpha]_D$ = +63; Compound **433**: $[\alpha]_D$ = -63.

EXAMPLE 188

(+)*R*-6-(2-Chloromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **434**, Structure **34** of Scheme VI, where R = chloromethyl, n = 1) and (-)*S*-6-(2-Chloromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **435**, Structure **34** of Scheme VI, where R = chloromethyl, n = 1)

Compound **434** was prepared in a similar synthetic sequence as that described in Examples **101** and **179** from Compound **309** (Structure **17** of Scheme III) and D-proline. Compound **434** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.90-12.10 (bs, 1H), 7.37 (d, J = 8.8,1H), 7.08 (s, 1H), 7.07 (s, 1H), 6.88 (s, 1H), 4.01-4.04 (m, 1H), 3.63 (dd, J = 2.4, 10.7,1H),), 3.54-3.57 (m, 1H), 3.31 (dd, J = 9.8, 11.2, 1H), 3.22-3.27 (m, 1H), 2.10-2.23 (m, 4H).

Compound **435** was prepared in the same fashion from Compound **309** and L-proline.

EXAMPLE 189

R-6-(2-Difluoromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **436**, Structure **34** of Scheme VI, where R = difluoromethyl, n = 1)

Compound **436** was prepared in a similar synthetic sequence as that described in Examples **101** and **179** from Compound **309** (Structure **17** of Scheme III) and D-proline and isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.80-12.00 (bs, 1H), 7.35 (d, J = 9.2, 1H), 7.13 (dd, J = 2.4, 9.2, 1H), 7.08 (s, 1H), 7.02 (s, 1H), 5.81 (dt, J = 3.6, 56.1, 1H), 4.03-4.09 (m, 1H), 3.66 (t, J = 7.9, 1H), 3.26 (q, J = 8.5, 1H), 2.04-2.28 (m, 4H).

EXAMPLE 190

(±)-6-(2*l*-(1*l*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **437**, Structure **36** of Scheme VI, where R = trifluoromethyl, n = 2) and (±)-6-(2*l*-(1*u*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **438**, Structure **36** of Scheme VI, where R = trifluoromethyl, n = 2)

(±)-6-(2-Formyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **439**, Structure **35** of Scheme VI, where R = formyl, n = 2)

Compound **439** was prepared from Compound **331** (Structure **33** of Scheme VI, where n = 2) by oxidation.

(±)-6-(2*l*-(1*l*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **437**, Structure **36** of Scheme VI, where R = trifluoromethyl, n = 2) and (±)-6-(2*l*-(1*u*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **438**, Structure **36** of Scheme VI, where R = trifluoromethyl, n = 2)

These compounds were prepared by the following General Procedure XVII from Compound **439**:

To the aldehyde (2.2 mmol) in THF (22 mL) at –78 °C was added the nucleophile or the $TMSCF_3$ (2.9 mmol, equiv). The reaction mixture was warmed to rt and stirred for 5-24 h. Work up involved quenching with H_20 and extraction with EA. The organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. by flash chromatography (EtOAc:hexane mixtures) afforded the desired products as diastereomers.

Compound **437** was isolated as yellow solid. ^1H NMR ($CDCl_3$, 500 MHz) 10.65 (bs, 1H), 7.37-7.28 (m, 3H), 7.08 (s, 1H), 4.35-4.32 (m, 1H), 4.11-3.94 (m, 1H), 3.65 (d, *J* = 15.6, 1H), 3.47 (s, 1H), 3.21-3.16 (m, 1H), 1.85-1.67 (m, 6H).

Compound **438** was isolated as yellow solid. ^1H NMR ($CDCl_3$, 500 MHz) 11.50 (bs, 1H), 7.37-7.35 (m, 3H), 7.08 (s, 1H), 4.19-4.10 (m, 1H), 3.82-3.81 (m, 1H), 3.25-3.22 (m, 2H), 2.48 (bs, 1H), 2.01-1.98 (m, 1H), 1.86-1.85 (m, 2H), 1.72-1.70 (m, 2H), 1.61-1.57 (m, 1H).

EXAMPLE 191

(±)-6-(2-Difluoromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **440**, Structure **34** of Scheme VI, where R = difluoromethyl, n = 2)

Compound **440** was prepared in a similar fashion as that described in Example **179** from Compound **439** (Structure **35** of Scheme VI, where n = 2) and isolated as yellow solid. ^1H NMR ($CDCl_3$, 500 MHz) 11.60-11.80 (bs, 1H), 7.31-7.33 (m, 2H), 7.25 (s, 1H), 7.08 (s, 1H), 5.90 (dt, *J* = 4.3, 55.8, 1H), 3.97-4.02 (m, 1H), 3.42 (d, *J* = 11.9, 1H), 3.24 (t, *J* = 10.7, 1H), 2.04-2.06 (m, 1H). 1.85-1.89 (m, 2H), 1.69-1.72 (m, 3H).

EXAMPLE 192

(±)-6-(2-Aminomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **441**, Structure **34** of Scheme VI, where R = aminomethyl, n = 2)

Compound **441** was prepared in a similar fashion as that described in Example **179** from Compound **439** (Structure **35** of Scheme VI, where n = 2) and isolated as yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) 7.37 (dd, J = 9.0, 2.5, 1H), 7.35 (d, J = 9.0, 1H), 7.24 (m, 1H), 7.07 (s, 1H), 3.70 (m, 1H), 3.32 (m, 1H), 3.12 (m, 1H), 2.92 (dd, J = 12.8, 5.9, 1H), 2.79 (dd, J = 12.8, 6.5, 1H), 1.85-1.65 (m, 6H).

EXAMPLE 193

(*R*)-6-(2-Vinyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **442**, Structure **34** of Scheme VI, where R = vinyl, n = 1)

Compound **442** was prepared in a similar fashion as that described in Example **179** from (*R*)-6-(2-Formyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **443**, Structure **35** of Scheme VI, where n = 1) and isolated as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) 11.17 (s, 1H), 7.24 (d, J = 8.9, 1H), 7.04 (s, 1H), 6.98 (dd, J = 8.9, 2.4, 1H), 6.90 (m, 1H), 5.81 (ddd, J = 16.2, 10.4, 5.8, 1H), 5.15 (dd, J = 10.4, 1.5, 1H), 5.14 (dd, J = 16.2, 1.5, 1H), 4.20 (m, 1H), 3.55 (td, J = 8.2, 2.9, 1H), 3.33 (q, J = 7.5, 1H), 2.21 (m, 1H), 2.06 (m, 2H), 1.91 (m, 1H).

EXAMPLE 194

(±)-6-(2-Vinyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **444**, Structure **34** of Scheme VI, where R = vinyl, n = 2)

Compound **444** was prepared in a similar fashion as that described in Example **179** from Compound **439** (Structure **35** of Scheme VI, where n = 2) and isolated as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) 11.20 (s, 1H), 7.31 (dd, J = 9.1, 2.5, 1H), 7.26 (d, J = 9.1, 1H), 7.25 (m, 1H), 7.04 (s, 1H), 5.78 (ddd, J = 17.3, 10.7, 6.6, 1H), 5.08 (dd, J = 10.7, 1.2, 1H), 5.05 (dd, J = 17.3, 1.2, 1H), 4.15 (m, 1H), 3.24-3.17 (m, 2H), 2.05-1.63 (m, 6H).

EXAMPLE 195

(±)-6-(2-Benzyloxyethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **445**, Structure **34** of Scheme VI, where R = benzyloxyethyl, n = 2)

Compound **445** was prepared by benzylation of Compound **343** (Structure **34** of Scheme VI, where R = 2-hydroxyethyl, n = 2) and isolated as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) 11.40 (s, 1H), 7.36-7.22 (m, 7H), 7.18 (m, 1H), 7.06 (s, 1H), 4.40 (d, J = 11.9, 1H), 4.38 (d, J = 11.9, 1H), 4.05 (m, 1H), 3.43 (dd, J = 9.2, 6.2, 1H), 3.40 (dd, J = 9.2, 6.4, 1H), 3.33 (dd, J = 11.9, 2.4, 1H), 3.05 (m, 1H), 1.92-1.63 (m, 8H).

EXAMPLE 196

(±)-6-(2-(2,2-Difluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **446**, Structure **34** of Scheme VI, where R = 2,2-difluoroethyl, n = 2)

Compound **446** was prepared from Compound ? (Structure ? of Scheme Va, where R =, n = 2) and isolated as yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) 10.95 (bs, 1H), 7.32 (dd, J = 9.0, 2.5, 1H), 7.28 (d, J = 9.0, 1H), 7.22 (m, 1H), 7.07 (s, 1H), 5.78 (tt, J = 56.4, 4.6, 1H), 4.08 (m, 1H), 3.34 (m, 1H), 3.03 (m, 1H), 2.12-1.65 (m, 8H).

EXAMPLE 197

(±)-6-(2-Trifluoroacetamidomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **447**, Structure **34** of Scheme VI, where R = trifluoroacetamidomethyl, n = 2)

Compound **447** was prepared by acetylation of Compound **441** (Structure **34** of Scheme VI, where R = aminomethyl, n = 2) and isolated as yellow solid. R_f = 0.32 (1:1 CH_2Cl_2: MeOH).

EXAMPLE 198

(±)-6-(2-(2-Ethoxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **448**, Structure **34** of Scheme VI, where R = 2-ethoxyethyl, n = 2)

Compound **448** was prepared by ethylation of Compound **343** (Structure **34** of Scheme VI, where R = 2-hydroxyethyl, n = 2) and isolated as yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) 11.86 (bs, 1H), 7.36 (dd, J = 9.3, 2.5 1H), 7.31 (d, J = 9.3, 1H), 7.17 (bs, 1H), 7.07 (s, 1H), 4.02 (m, 1H), 3.40-3.31 (m, 5H), 3.06 (m, 1H), 1.90-1.62 (m, 8H), 1.15 (t, J = 7.0, 3H).

EXAMPLE 199

(±)-6-(2-(4-Trifluoromethyl)benzyloxyethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 449, Structure 34 of Scheme VI, where R = 4-trifluoromethylbenzyloxyethyl, n = 2)

Compound **449** was prepared by benzylation of Compound **343** (Structure **34** of Scheme VI, where R = 2-hydroxyethyl, n = 2) and isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.00-11.20 (bs, 1H), 7.58 (d, *J* = 8.2, 2H), 7.38 (d, *J* = 7.9, 2H), 7.31-7.33 (m, 1H), 7.22 (d, *J* = 8.2, 1H), 7.18 (bs, 1H), 7.05 (s, 1H), 4.43 (s, 2H), 4.05-4.09 (m, 1H), 3.44 (q, *J* = 6.7, 2H), 3.33 (d, *J* = 11.9, 1H), 3.05-3.08 (m, 1H), 1.63-1.96 (m, 8H).

EXAMPLE 200

(+)-6-(2*R*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 450, Structure 36 of Scheme VI, where R = trifluoromethyl, n = 1) and (-)6-(2*R*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 451, Structure 36 of Scheme VI, where R = trifluoromethyl, n = 1)

Compounds **450** and **451** were prepared in a similar synthetic sequence as that described in Example **190** from Compound **309** (Structure **17** of Scheme III) and D-proline. Compound **450** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 10.10 (bs, 1H), 7.16-7.07 (m, 2H), 7.03 (s, 1H), 6.99 (s, 1H), 4.14 (d, *J* = 6.8, 1H), 3.79 (d, *J* = 6.8, 1H), 3.66-3.61 (m, 1H), 3.21-3.18 (m, 2H), 2.19-2.04 (m, 4H). Compound **451** was also isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.05 (bs, 1H), 7.28 (d, *J* = 8.9, 1H), 7.04-7.01 (m, 2H), 6.89 (s, 1H), 4.40-4.39 (m, 1H), 4.14 (d, *J* = 7.3, 1H), 3.65 (dt, *J* = 8.2, 3.7, 1H), 3.25 (q, *J* = 7.9, 1H), 2.56 (s, 1H), 2.47-2.44 (m, 1H), 2.28-2.23 (m, 1H), 2.15-2.01 (m, 2H).

EXAMPLE 201

6-(2*S*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 452, Structure 36 of Scheme VI, where R = trifluoromethyl, n = 1) and 6-(2*S*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 453, Structure 36 of Scheme VI, where R = trifluoromethyl, n = 1)

Compounds **452** and **453** were prepared in a similar synthetic sequence as that described in Example **190** from Compound **309** (Structure **17** of Scheme III) and L-proline. Compounds **452** and **453** were isolated as yellow solid.

EXAMPLE 202

(±)-6-(2*l*-(1*l*-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **454**, Structure **36** of Scheme VI, where R = methyl, n = 2) and (±)-6-(2*l*-(1*u*-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **455**, Structure **36** of Scheme VI, where R = methyl, n = 2)

These compounds were prepared in a similar fashion as that described in Example **190**, General Procedure XVII from Compound **439** and methyl anion.

Compound **454** was isolated as yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) 10.00-10.20 (bs, 1H), 7.36 (dd, J = 2.4, 8.8, 1H), 7.32 (s, 1H), 7.20 (d, J = 9.3, 1H), 7.06 (s, 1H), 4.25-4.30 (m, 1H), 3.59 (d, J = 14.0, 1H), 3.41-3.44 (m, 1H), 3.31-3.36 (m, 1H), 2.75 (bs, 1H), 1.60-1.75 (m, 6H), 1.29 (d, J = 5.9, 3H).

Compound **455** was isolated as yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) 10.50-10.60 (bs, 1H), 7.38-7.40 (m, 1H), 7.30 (d, J = 9.3, 1H), 7.07 (s, 1H), 3.95-3.98 (m, 1H), 3.23-3.25 (m, 1H), 3.11-3.25 (m, 2H), 1.84-1.94 (m, 3H), 1.67-1.78 (m, 4H), 1.10 (d, J = 6.3, 3H).

EXAMPLE 203

(-)-6-(2*S*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **456**, Structure **36** of Scheme VI, where R = trifluoromethyl, n = 2) and (+)-6-(2*R*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **457**, Structure **36** of Scheme VI, where R = trifluoromethyl, n = 2)

Compounds **456** ($[\alpha]_D$ = -28) and **457** ($[\alpha]_D$ = +28) were prepared by chiral HPLC separation of Compound **438**.

EXAMPLE 204

(-)-6-(2*S*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **459**, Structure **36** of Scheme VI, where R = trifluoromethyl, n = 2) and (+)-6-(2*R*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **458**, Structure **36** of Scheme VI, where R = trifluoromethyl, n = 2)

Compounds **458** ($[\alpha]_D$ = +50) and **459** ($[\alpha]_D$ = -51) were prepared by chiral HPLC separation of Compound **437**.

EXAMPLE 205

(±)-6-(2*l*-(1*l*-Acetyloxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 460, Structure 37 of Scheme VI, where R^1 = acetyl, R = methyl, n = 2)

This compound was prepared by acetylation of Compound **454** (Structure **36** of Scheme VI, where R = methyl, n = 2) and isolated as yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) 10.80-11.00 (bs, 1H), 7.38-7.31 (m, 1H), 7.23 (d, *J* = 9.3, 1H), 7.12 (s, 1H), 7.05 (s, 1H), 5.49-5.55 (m, 1H), 3.83-3.87 (m, 1H), 3.35 (d, *J* = 13.2,1H), 3.21-3.26 (m, 1H), 1.64-1.81 (m, 6H), 1.50 (s, 3H), 1.22 (d, *J* = 6.3, 3H).

EXAMPLE 206

(±)-6-(2*l*-(1*u*-Acetyloxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 461, Structure 37 of Scheme VI, where R^1 = acetyl, R = methyl, n = 2)

This compound was prepared by acetylation of Compound **455** (Structure **36** of Scheme VI, where R = methyl, n = 2) and isolated as yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.80-12.00 (bs, 1H), 7.32 (d, *J* = 9.3, 1H), 7.26-7.28 (m, 1H), 7.19 (s, 1H), 7.07 (s, 1H), 5.37-5.40 (m, 1H), 3.75-3.76 (m, 1H), 3.40-3.46 (m, 1H), 3.12-3.17 (m, 1H), 1.59-1.81 (m, 9H), 1.14 (d, *J* = 6.3, 3H).

EXAMPLE 207

(±)-6-(2*l*-(1*u*-Methoxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 462, Structure 37 of Scheme VI, where R^1 = methyl, R = trifluoromethyl, n = 2)

This compound was prepared by methylation of Compound **438** (Structure **36** of Scheme VI, where R = trifluoromethyl, n = 2) and isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 12.00-12.40 (bs, 1H), 7.37-7.39 (m, 2H), 7.27-7.29 (m, 1H), 7.13 (s, 1H), 3.99 (q, *J* = 4.9, 1H), 3.76-3.80 (m, 1H), 3.53 (s, 3H), 3.44 (dt, *J* = 4.0, 13.4, 1H), 3.24-3.29 (m, 1H), 2.01-2.08 (m, 1H), 1.61-1.86 (m, 5H).

EXAMPLE 208

(±)-6-(2*l*-(1*l*-Methoxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 463, Structure 37 of Scheme VI, where R^1 = methyl, R = trifluoromethyl, n = 2)

This compound was prepared by methylation of Compound **437** (Structure **36** of Scheme VI, where R = trifluoromethyl, n = 2) and isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz)

12.00-12.40 (bs, 1H), 7.34-7.39 (m, 2H), 7.20 (s, 1H), 7.10-7.15 (bs, 1H), 4.14-4.17 (m, 1H), 3.89-3.94 (m, 1H), 3.57 (d, *J* = 13.4, 1H), 3.35 (s, 3H), 3.19 (dt, *J* = 3.0, 13.4, 1H), 1.61-1.89 (m, 6H).

EXAMPLE 209

7-Methoxy-6-(N-methyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **464**, Structure **41** of Scheme VII, where R = methyl)

2-Methoxy-N-2,2,2-trifluoroethyl-4-nitroaniline (Compound **465**):

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using 2-amino-5-nitroanisole and trifluoroacetaldehyde hydrate in place of Compound **200** and propionaldehyde. Compound **465** was isolated as a light brown crystalline solid after recrystallization (1:1 EtOAc:hexanes, 30 mL): R_f 0.52 (2:1 hexanes:EtOAc); ^{1}H NMR (400 MHz, acetone-d_6) 7.87 (dd, *J* = 8.9, 2.4, 1 H), 7.69 (d, *J* = 2.4, 1 H), 6.96 (d, *J* = 8.9, 1 H), 6.38 (broad s, 1 H), 4.20 (qd, *J* = 9.3, 7.1, 2 H), 4.00 (s, 3 H).

4-Amino-2-methoxy-N-2,2,2-trifluoroethylaniline (Compound **466**, Structure **39** of Scheme VII):

This compound was prepared by General Procedure III in Example 1 from Compound **465** (8.40 g, 33.6 mmol), zinc dust (9.66 g, 0.148 mmol), and calcium chloride dihydrate (10.9 g, 73.9 mmol) in 300 mL 95% EtOH/water. Compound **466** was isolated in 90% (6.7 g) yield as a deep purple oil: R_f 0.25 (1:1 hexanes:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) 6.54 (d, *J* = 8.1, 1 H), 6.20-6.30 (m, 2 H), 4.15 (broad s, 1 H), 3.81 (s, 3 H), 3.68 (qd, *J* = 9.0, 7.4, 2 H), 3.38 (broad s, 2 H).

7-Methoxy-6-(N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **467**, Structure **40** of Scheme VII):

This compound was prepared according to General Procedure I in Example 1 from Compound **466** (5.72 g, 26.0 mmol) and 4,4,4 trifluoroacetoacetate (4.56 mL, 5.74 g, 31.2 mmol) in 87 mL toluene, followed by treatment with 65 mL concentrated H_2SO_4. Compound **467** was isolated as a fluffy yellow solid: R_f 0.19 (4:1 EtOAc:CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6)

10.87 (broad s, 1 H), 7.04 (s, 1 H), 6.99 (broad s, 1 H), 6.73 (s, 1 H), 5.54 (broad m, 1 H), 4.07 (app quint, J = 8.4, 2 H), 3.98 (s, 3 H).

7-Methoxy-6-(N-methyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **464**, Structure **41** of Scheme VII, where R = methyl):

A solution of Compound **467** (24 mg, 0.070 mmol) and paraformaldehyde (21 mg, 0.70 mmol) in 1.4 mL acetic acid was stirred for 15 min, whereupon $NaBH_3CN$ (22 mg, 0.35 mmol) was added. After 18 h, the mixture was partitioned between EtOAc (40 mL) and sat'd $NaHCO_3$ (40 mL). The organic layer was washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated. Flash chromatography (4:1 EtOAc:CH_2Cl_2) afforded 20 mg (81%) of Compound **464** as a yellow solid: R_f 0.38 (4:1 EtOAc: CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) 12.9 (broad s, 1 H), 7.37 (broad s, 1 H), 6.96 (s, 1 H), 6.89 (s, 1 H), 4.04 (s, 3 H), 3.83 (q, J = 9.3, 2 H), 3.06 (s, 3 H).

EXAMPLE 210

7-Methoxy-6-(N-ethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **468**, Structure **41** of Scheme VII, where R = ethyl)

A solution of Compound **467** (Structure **40** of Scheme VII) (10 mg, 0.030 mmol) and acetaldehyde (13 mg, 0.30 mmol) in 1 mL acetic acid was stirred for 20 min, whereupon $NaBH_3CN$ (9.4 mg, 0.15 mmol) was added. After 18 h, the mixture was partitioned between EtOAc (30 mL) and sat'd $NaHCO_3$ (30 mL). The organic layer was washed with brine (20 mL), dried over $MgSO_4$, filtered and concentrated. Flash chromatography (3:2 EtOAc:CH_2Cl_2) afforded 4.5 mg (41%) of Compound **468** as a yellow solid: R_f 0.40 (3:2 EtOAc: CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) 12.7 (broad s, 1 H), 7.45 (broad s, 1 H), 6.95 (s, 1 H), 6.88 (s, 1 H), 4.02 (s, 3 H), 3.76 (q, J = 9.4, 2 H), 3.33 (q, J = 7.1, 2 H), 1.08 (t, J = 7.0, 3 H).

EXAMPLE 211

7-Hydroxy-6-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 469, Structure 42 of Scheme VII, where R = H)

A suspension of Compound **467** (Structure **40** of Scheme VII) (34 mg, 0.10 mmol), NaH (60% mineral oil suspension, 16 mg, 0.40 mmol) and thiophenol (48 mg, 0.44 mmol) in 1.5 mL DMF was heated at 80 °C for 7 h. The mixture was poured into cold sat'd NH_4Cl (30 mL), and the aqueous layer was extracted with EtOAc (2x 30 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (9:1 CH_2Cl_2:MeOH) afforded 13 mg (39%) of Compound **469** as a yellow solid: R_f 0.17 (9:1 CH_2Cl_2:MeOH); ^1H NMR (400 MHz, acetone-d_6) 10.9 (broad s, 1 H), 9.8 (v broad s, 1 H), 7.00 (s, 2 H), 6.68 (s, 1 H), 5.38-5.48 (m, 1 H), 4.02-4.12 (m, 2 H).

EXAMPLE 212

6-(N-Cyclopropylmethyl-N-2,2,2-trifluoroethyl)amino-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 470, Structure 41 of Scheme VII, where R = cyclopropylmethyl)

This compound was prepared according to General Procedure IV in Example 2 from Compound **467** (Structure **40** of Scheme VII) (33 mg, 0.097 mmol), cyclopropanecarboxaldehyde (34 mg, 0.48 mmol) and $NaBH_3CN$ (37 mg, 0.59 mmol) in 1 mL trifluoroacetic acid to afford 38 mg (96%) of Compound **470** as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) 11.0 (broad s, 1 H), 7.46 (broad s, 1 H), 6.86 (s, 1 H), 6.74 (s, 1 H), 3.88 (s, 3 H), 3.84 (q, J = 9.3, 2 H), 3.08 (d, J = 6.6, 2 H), 0.80-0.90 (m, 1 H), 0.40-0.50 (m, 2 H), 0.07-0.13 (m, 2 H).

EXAMPLE 213

6-(N-Cyclopropylmethyl-N-2,2,2-trifluoroethyl)amino-7-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 471, Structure 42 of Scheme VII, where R = cyclopropylmethyl)

A suspension of Compound **470** (35 mg, 0.089 mmol), NaH (60% mineral oil suspension, 28 mg, 0.71 mmol) and thiophenol (83 mg, 0.76 mmol) in 1.3 mL DMF was heated at 105 °C for 4h. The mixture was poured into cold water (20 mL) and neutralized with 2N $NaHSO_4$. The

aqueous layer was extracted with EtOAc (2x 20 mL), and the combined organic layers were washed with water (20 mL), brine (10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (7:3 EtOAc:CH_2Cl_2) afforded 14 mg (42%) of Compound **471** as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 12.3 (broad s, 1 H), 7.60 (broad s, 2 H), 7.03 (s, 1 H), 6.93 (s, 1 H), 3.64 (q, J = 8.9, 2 H), 2.94 (d, J = 6.9, 2 H), 0.75-0.85 (m, 1 H), 0.42-0.52 (m, 2 H), 0.05 (m, 2 H).

EXAMPLE 214

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 472, Structure 41 of Scheme VII, where R = isobutyl)

This compound was prepared according to General Procedure IV in Example 2 from Compound **467** (Structure **40** of Scheme VII) (34 mg, 0.10 mmol), isobutyraldehyde (36 mg, 0.50 mmol) and $NaBH_3CN$ (38 mg, 0.60 mmol) in 1 mL trifluoroacetic acid to afford 24 mg (61%) of Compound **472** as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 12.0 (broad s, 1 H), 7.47 (broad s, 1 H), 6.93 (s, 1H), 6.82 (s, 1 H), 4.00 (s, 3 H), 3.73 (q, J = 9.3, 2 H), 3.04 (d, J = 7.2, 2 H), 1.60-1.70 (m, 1H), 0.88 (t, J = 6.6, 6 H).

EXAMPLE 215

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-7-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 473, Structure 42 of Scheme VII, where R = isobutyl)

A suspension of Compound **472** (Structure **41** of Scheme VII, where R = isobutyl) (19 mg, 0.048 mmol), NaH (60% mineral oil suspension, 15 mg, 0.38 mmol) and thiophenol (45 mg, 0.41 mmol) in 1.5 mL DMF was heated at 105 °C for 4h. The mixture was poured into cold water (20 mL) and neutralized with 2N $NaHSO_4$. The aqueous layer was extracted with EtOAc (2 x 20 mL), and the combined organic layers were washed with water (20 mL), brine (10 mL), dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (7:3 EtOAc:CH_2Cl_2) afforded 8.5 mg (46%) of Compound **473** as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 12.1 (broad s, 1 H), 7.60 (s, 1 H), 7.43 (broad s, 1 H), 7.02 (s, 1 H), 6.92 (s, 1 H), 3.53 (q, J = 8.9, 2 H), 2.93 (d, J = 7.0, 2 H), 1.55-1.65 (m, 1 H), 0.93 (d, J = 6.6, 6 H).

EXAMPLE 216

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound 474, Structure 45 of Scheme VIII, where $R^5 = R^6$ = 2,2,2-trifluoroethyl)

6-Amino-4-trifluoromethylcoumarin (Compound **475**, Structure **44** of Scheme VIII):

This compound was prepared in a similar fashion as that described in Example 1, General Procedures I, II and III but using phenol in place of aniline. Compound **475** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 7.21 (d, J = 8.8, 1 H), 7.10 (dd, J = 8.8, 2.4, 1 H), 7.00 (s, 1 H), 6.81 (s, 1 H), 5.09 (bs, 2 H).

6-(bis-2,2,2-Trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound **474**, Structure **45** of Scheme VIII, where $R^5 = R^6$ = 2,2,2-trifluoroethyl):

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **475** and TFA in place of Compound **200** and difluoroacetic acid. Compound **474** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 7.37 (d, J = 9.3, 1 H), 7.23 (dd, J = 9.3, 2.9, 1 H), 7.20 (s, 1 H), 6.83 (s, 1 H), 4.07 (q, $J_{H\text{-}F}$ = 8.3, 4 H).

EXAMPLE 217

(±)-3,4-Dihydro-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound 476, Structure 46 of Scheme VIII, where $R^5 = R^6$ = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compound **474** (Structure **45** of Scheme VIII, where $R^5 = R^6$ = 2,2,2-trifluoroethyl). Compound **476** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 7.07 (d, J=8.8, 1 H), 6.98 (dd, J=8.8, 2.9, 1 H), 6.82 (d, J = 2.9, 1 H), 4.07-3.97 (m, 4 H), 3.67-3.64 (m, 1 H), 3.15 (dd, J = 17.1, 1.9, 1 H), 2.95 (dd, J = 17.1, 7.3, 1 H).

EXAMPLE 218

6-(N-2,2,2-Trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound 477, Structure 45 of Scheme VIII, where R^5 = H, R^6 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **475** (Structure **44** of Scheme VIII) and trifluoroacetyraldehyde. Compound **477** was isolated as a yellow solid: ^{1}H NMR (500 MHz,

$CDCl_3$) 7.29 (d, J = 8.8, 1 H), 6.99 (dd, J = 8.8, 2.9, 1 H), 6.92 (s, 1 H), 6.80 (s, 1 H), 4.15 (t, J = 6.3, 1 H), 3.84-3.78 (m, 2 H).

EXAMPLE 219

6-(N-Isopropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound 478, Structure 45 of Scheme VIII, where R^5 = isopropyl, R^6 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV from Compound **475** (Structure **44** of Scheme VIII) by using acetone and trifluoroacetyraldehyde sequentially. Compound **478** was isolated as a yellow solid: ^1H NMR (500 MHz, $CDCl_3$) 7.33 (d, J = 9.3, 1 H), 7.24 (dd, J = 9.3, 2.9, 1 H), 7.18 (s, 1 H), 6.79 (s, 1 H), 4.01-3.96 (m, 1 H), 3.80 (q, J_{H-F} = 8.8, 2 H), 1.24 (d, J = 6.8, 6 H).

EXAMPLE 220

6-N-Isobutylamino-4-trifluoromethylcoumarin (Compound 479, Structure 45 of Scheme VIII, where R^5 = isobutyl, R^6 = H)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV from Compound **475** (Structure **44** of Scheme VIII) and isobutyraldehyde. Compound **479** was isolated as a yellow solid: ^1H NMR (500 MHz, $CDCl_3$) 7.22 (d, J = 8.8, 1 H), 6.88 (dd, J = 8.8, 2.4, 1 H), 6.75 (s, 2 H), 3.89 (bs, 1 H), 2.95 (d, J = 6.4, 2 H), 1.94-1.88 (m, 1 H), 1.02 (d, J = 6.8, 6 H).

EXAMPLE 221

6-N,N-Diethylamino-4-trifluoromethylcoumarin (Compound 480, Structure 45 of Scheme VIII, where R^5 = R^6 = methyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV from Compound **475** (Structure **44** of Scheme VIII) and acetaldehyde. Compound **480** was isolated as a yellow solid: ^1H NMR (500 MHz, $CDCl_3$) 7.27 (d, J = 9.3, 1 H), 6.99 (dd, J = 9.3, 2.9, 1 H), 6.82 (s, 1 H), 6.76 (s, 1 H), 3.89 (q, J = 7.3, 4 H), 1.19 (t, J = 7.3, 6 H).

EXAMPLE 222

6-N,N-Dipropylamino-4-trifluoromethylcoumarin (Compound **481**, Structure **45** of Scheme VIII, where $R^5 = R^6$ = propyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV from Compound **475** (Structure **44** of Scheme VIII) and propionaldehyde. Compound **481** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 7.25 (d, J = 9.3, 1 H), 6.94 (dd, J = 9.3, 2.9, 1 H), 6.77 (s, 1 H), 6.75 (s, 1 H), 3.27 (t, J = 7.3, 4 H), 1.65-1.57 (m, 4 H), 0.95 (t, J = 7.3, 6 H).

EXAMPLE 223

6-N-Propylamino-4-trifluoromethylcoumarin (Compound **482**, Structure **45** of Scheme VIII, where R^5 = H, R^6 = propyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV from Compound **475** (Structure **44** of Scheme VIII) and propionaldehyde. Compound **482** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 7.23(d, J = 8.8, 1 H), 6.89 (dd, J = 8.8, 2.4, 1 H), 6.77 (s, 1 H), 6.76 (s, 1 H), 3.82 (bs, 1 H), 3.10 (t, J = 7.3, 2 H), 1.71-1.64 (m, 2 H), 1.03 (t, J = 7.3, 3 H).

EXAMPLE 224

6-(N-Isobutyl-N-propylamino)-4-trifluoromethylcoumarin (Compound **483**, Structure **45** of Scheme VIII, where R^5 = isobutyl, R^6 = propyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV from Compound **475** (Structure **44** of Scheme VIII) by using propionaldehyde and isobutyraldehyde. Compound **483** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 7.25(d, J = 9.3, 1 H), 6.95 (dd, J = 9.3, 2.9, 1 H), 6.78 (s, 1 H), 6.75 (s, 1 H), 3.30 (t, J = 7.8, 2 H), 3.11 (d, J = 7.3, 2 H), 2.05-1.99 (m, 1 H), 1.63-1.57 (m, 2 H), 0.95-0.93 (m, 9 H).

EXAMPLE 225

6-(N-2,2,2-Trifluoroethyl-N-propylamino)-4-trifluoromethylcoumarin (Compound **484**, Structure **45** of Scheme VIII, where R^5 = 2,2,2-trifluoroethyl, R^6 = propyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV from Compound **475** (Structure **44** of Scheme VIII) by using propionaldehyde and

trifluoroacetaldehyde. Compound **484** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 7.31 (d, J = 9.3, 1 H), 7.08 (dd, J = 9.3, 2.9, 1 H), 6.98 (s, 1 H), 6.79 (s, 1 H), 3.89 (q, J_{H-F}=8.8, 2 H), 3.47 (t, J = 7.8, 2 H), 1.68-1.63 (m, 2 H), 0.96 (t, J = 7.3, 3 H).

EXAMPLE 226

1,4-Dihydro-4,4-dimethyl-6-methylamino-1,3-benzo[d]oxazin-2-one (Compound 485, Structure 52 of Scheme IX, where $R^1 = R^2 = R^4$ = methyl, R^5 = H, W = oxygen)

1,4-Dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **486**, Structure **49** of Scheme IX, where $R^1 = R^2$ = methyl, W = oxygen):

To a solution of 2-isopropenyl aniline (Structure **47** of Scheme IX, where R^1 = methyl) (1 mL, 7.3 mmol) and dry methylene chloride (20 mL) was slowly added methylchloroformate (0.62 mL, 8.1 mmol). To this solution was added DMAP (0.9 g, 8.1 mmol) in methylene chloride (5 mL). Stirred at room temperature for 15 hrs. Partitioned reaction mixture between EtOAc (20 mL) and H_2O (5 mL). Washed organic layer with brine (3 x 10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to afford crude as a colorless oil. Purified by silica flash chromatography (10% Hex/EtOAc) to afford 1.3 g of 2-isopropenyl-N-methylcarbamate aniline in 94% yield as a colorless oil. This product was dissolved in dichloroethane (20 mL) and treated with p-TsOH (1.4 g) then heated to reflux. After 2 hrs. the reaction mixture was quenched with saturated $NaHCO_3$ and extracted with EtOAc (20 mL). The organic layer was washed with brine (3 x 10 mL), dried (Na_2SO_4), and concentrated *in vacuo*. Purified by silica flash chromatography (50% Hex/EtOAc) to afford 1.1 g of Compound **486** in 92% yield as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.70 (br s, 1 H), 7.22 (t, J = 7.9, 1 H), 7.13 (d, J = 7.9, 1 H), 7.05 (t, J = 7.9, 1 H), 6.86 (d, J = 7.9, 1 H), 1.71 (s, 6 H).

6-Amino-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **487**, Structure **51** of Scheme IX, where $R^1 = R^2$ = methyl, W = oxygen):

To a solution of Compound **486** (50 mg, 0.28 mmol) and conc. H_2SO_4 (2 mL), chilled to 0 °C, was added fuming HNO_3 (0.03 mL). After 15 min. poured reaction mixture onto ice and extracted with EtOAc (5 mL), washed with H_2O (5 x 1 mL) and brine (5 x 1 mL) then dried (Na_2SO_4) and concentrated *in vacuo* to afford the crude product as a yellow solid. Dissolved in 2:1 EtOAc/MeOH (5 mL) and hydrogenated over 10% Pd/C (10 mg) at rt and 1 atm. After 15 hrs. filtered through plug of silica gel to afford 50 mg of Compound **487** in 90% yield as a white

solid: ^1H NMR (400 MHz, acetone-d_6) 9.00 (br s, 1 H), 6.93 (d, J = 8.0, 1 H), 6.60 (m, 2 H), 1.64 (s, 6 H).

1,4-Dihydro-4,4-dimethyl-6-methylamino-1,3-benzo[d]oxazin-2-one (Compound **485**, Structure **52** of Scheme IX, where $R^1 = R^2 = R^4$ = methyl, R^5 = H, W = oxygen):

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **487** and paraformaldehyde in place of Compound **200** and propionaldehyde. Compound **485** was isolated as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) 7.82 (bs, 1 H), 6.66 (d, J = 8.5, 1 H), 6.52 (dd, J = 8.5, 2.1, 1 H), 6.39 (d, J = 2.1, 1 H), 2.83 (s, 3 H), 1.69 (s, 6 H).

EXAMPLE 227

1,4-Dihydro-4,4-dimethyl-6-dimethylamino-1,3-benzo[d]oxazin-2-one (Compound **488**, Structure **52** of Scheme IX, where $R^1 = R^2 = R^4 = R^5$ = methyl, W = oxygen)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII from Compound **487** (Structure **51** of Scheme IX, where $R^1 = R^2$ = methyl, W = oxygen) (15 mg, 0.08 mmol) and paraformaldehyde (30mg) to afford 5 mg (28%) of Compound **488** as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 7.66 (br s,1 H), 6.69 (d, J = 8.6, 1 H), 6.65 (dd, J = 2.5, 8.6, 1 H), 6.50 (d, J = 2.5, 1 H), 2.92 (s, 6 H), 1.71 (s, 6 H).

EXAMPLE 228

1,4-Dihydro-4,4-dimethyl-6-dipropylamino-1,3-benzo[d]oxazin-2-one (Compound **489**, Structure **52** of Scheme IX, where $R^1 = R^2$ = methyl, $R^4 = R^5$ = propyl, W = oxygen)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using Compound **487** (Structure **51** of Scheme IX, where $R^1 = R^2$ = H, W = oxygen) and propionaldehyde in place of Compound **200** and paraformaldehyde. Compound **489** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 7.52 (br s, 1 H), 6.64 (d, J = 8.5, 1 H), 6.53 (dd, J = 2.5, 8.5, 1 H), 6.39 (d, J = 2.5, 1 H), 3.19 (t, J = 7.5, 1 H), 1.55 (m, 10 H), 0.92 (t, J = 7.5, 1 H).

EXAMPLE 229

1,4-Dihydro-4,4-dimethyl-6-(bis-N,N-2,2,2-trifluoroethyl)amino-1,3-benzo[d]oxazin-2-one (Compound **490**, Structure **52** of Scheme IX, where $R^1 = R^2$ = methyl, $R^4 = R^5$ = 2,2,2-trifluoroethyl, W = oxygen)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using Compound **487** (Structure **51** of Scheme IX, where $R^1 = R^2$ = H, W = oxygen) and trifluoroacetaldehyde in place of Compound **200** and paraformaldehyde. Compound **490** was isolated as an orange oil: ^{1}H NMR (400 MHz, $CDCl_3$) 8.05 (brs, 1 H), 6.85 (dd, *J* = 2.6, 8.7, 1 H), 6.75 (d, *J* = 8.7, 1 H), 6.71 (d, *J* = 2.6, 1 H), 3.95 (q, *J* = 8.6, 4 H), 1.70 (s, 6 H).

EXAMPLE 230

1,4-Dihydro-4,4-dimethyl-6-(N-2,2,2-trifluoroethyl)amino-1,3-benzo[d]oxazin-2-one (Compound **491**, Structure **52** of Scheme IX, where $R^1 = R^2$ = methyl, R^4 = 2,2,2-trifluoroethyl, R^5 = H, W = oxygen)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **487** (Structure **51** of Scheme IX, where $R^1 = R^2$ = H, W = oxygen) and trifluoroacetaldehyde in place of Compound **200** and propionaldehyde. Compound **491** was isolated as a white solid; ^{1}H NMR (400 MHz, $CDCl_3$) 8.16 (brs, 1 H), 6.70 (d, *J* = 8.5, 1 H), 6.59 (dd, *J* = 2.6, 8.5, 1 H), 6.47 (d, *J* = 2.6, 1 H), 3.80 (brs, 1 H), 3.73 (q, *J* = 8.9, 2 H), 1.69 (s, 6 H).

EXAMPLE 231

(±)-1,4-Dihydro-4-methyl-6-diallylamino-1,3-benzo[d]oxazin-2-one (Compound **492**, Structure **52** of Scheme IX, where R^1 = methyl, R^2 = H, $R^4 = R^5$ = allyl, W = oxygen)

(±)-1,4-Dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **493**, Structure **49** of Scheme IX, where R^1 = methyl, R^2 = H, W = oxygen):

To a solution of 2-N-(*tert*-butoxycarbonyl)amino-(2-hydroxyethyl)benzene (0.58 g, 2.4 mmol) and dichloroethane (10 mL) was added TsOH (0. 5g, 2.6 mmol) and the reaction mixture was heated to reflux. After 20 minutes the reaction was quenched with saturated $NaHCO_3$ (10 mL) and extracted with EtOAc (20 mL). The organic layer was washed with brine (3x 5 mL),

dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by flash chromatography (50% EtOAc/hex) to afford 0.3 g (75%) of Compound **493** as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 8.64 (br s, 1 H), 7.27 (t, J = 7.8, 1 H), 7.08 (d overlapping t, 2 H), 6.86 (d, J = 7.8, 1 H), 5.50 (q, J = 6.7, 1 H), 1.71 (d, J = 6.7, 3 H).

(±)-6-Amino-1,4-dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **494**, Structure **51** of Scheme IX, where R^1 = methyl, R^2 = H, W = oxygen):

To a solution of Compound **493** (130 mg, 0.8 mmol) and conc. H_2SO_4 (3 mL), chilled to 0 °C, was added fuming HNO_3 (0.06 mL). After 15 min. poured reaction mixture onto ice and extracted with EtOAc (5 mL), washed with H_2O (5x 1 mL) and brine (5 x 1 mL) then dried (Na_2SO_4) and concentrated *in vacuo* to afford the crude product as a yellow solid. Dissolved in 2:1 EtOAc/MeOH (5 mL) and hydrogenated over 10% Pd/C (10 mg) at rt and 1 atm. After 15 hrs. filtered through plug of silica gel and purified by PTLC (20x20 cm, 1000 μm, 50 % EtOAc/hex) to afford 100 mg of Compound **494** (70%) as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) 8.47 (br s, 1 H), 6.66 (d, J = 8.3, 1 H), 6.59 (dd, J = 2.2, 8.3, 1 H), 6.43 (d, J = 2.2, 1 H), 5.40 (q, J = 6.6, 1 H), 3.63 (br s, 2 H), 1.67 (d, J = 6.6, 1 H).

1,4-Dihydro-4-methyl-6-diallylamino-1,3-benzo[d]oxazin-2-one (Compound **492**, Structure **52** of Scheme IX, where R^1 = methyl, R^2 = H, R^4 = R^5 = allyl, W = oxygen)

This compound was prepared in a similar fashion as that described in Example 77, General Procedure IX but using Compound **494** in place of Compound **200**. Compound **492** was isolated as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$) 6.66 (d, J = 8.6, 1 H), 6.60 (dd, J = 2.5, 8.6, 1 H), 6.42 (d, J = 2.5, 1 H), 5.82 (m, 2 H), 5.43 (q, J = 6.7, 1 H), 5.16 (m, 4 H), 3.88 (m, 4 H), 1.65 (d, J = 6.7, 3 H).

EXAMPLE 232

6-Amino-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **495**, Structure **51** of Scheme IX, where R^1 = R^2 = methyl, W = carbon)

To a solution of 3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **496**, Structure **49** of Scheme IX, where R^1 = R^2 = methyl, W = carbon) (0.50 g, 2.8 mmol) and conc. H_2SO_4 (10 mL), chilled to 0 °C, was added fuming HNO_3 (0.12 mL). After 15 min. poured reaction mixture onto ice and extracted with EtOAc (20 mL), washed with H_2O (5 x 5 mL) and brine (5 x 5 mL)

then dried (Na_2SO_4) and concentrated *in vacuo* to afford the crude product as a yellow solid. Dissolved in 9:1 EtOAc/MeOH (20 mL) and hydrogenated over 10% Pd/C (50 mg) at room temperature and 1 atm. After 15 hrs. filtered through plug of silica gel to afford Compound **495** (0.48 g) in 89% yield as an orange solid: ^1H NMR (400 MHz, $CDCl_3$) 7.67 (br s, 1 H), 6.66 (d, *J* = 2.3, 1H), 6.57 (d, *J* = 8.3, 1 H), 6.51 (dd, *J* = 2.3, 8.3, 1 H), 3.57 (br s, 2 H), 2.43 (s, 2 H), 1.28 (s, 6 H).

EXAMPLE 233

6-Diallylamino-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound 497, Structure 52 of Scheme IX, where $R^1 = R^2$ = methyl, $R^4 = R^5$ = allyl, W = carbon)

This compound was prepared in a similar fashion as that described in Example 77, General Procedure IX but using Compound **495** (Structure **51** of Scheme IX, where $R^1 = R^2$ = methyl, W = carbon) in place of Compound **200**. Compound **497** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 7.40 (br s, 1 H), 6.66 (d, *J* = 2.7, 1 H), 6.59 (d, *J* = 8.0, 1 H), 6.52 (dd, *J* = 2.7, 8.0, 1 H), 5.90 to 5.81 (m, 2 H), 5.21 to 5.16 (m, 4 H), 3.89 (d, *J* = 5.0, 4 H), 2.43 (s, 2 H), 1.29 (s, 6 H).

EXAMPLE 234

3,4-Dihydro-4,4-dimethyl-6-dipropylamino-2(1*H*)-quinolinone (Compound 498, Structure 52 of Scheme IX, where $R^1 = R^2$ = methyl, $R^4 = R^5$ = propyl, W = carbon)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using Compound **495** (Structure **51** of Scheme IX, where $R^1 = R^2$ = methyl, W = carbon) and propionaldehyde in place of Compound **200** and paraformaldehyde. Compound **498** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 7.77 (br s, 1 H), 6.62 (d, *J* = 8.6, 1 H), 6.60 (d, *J* = 2.7, 1 H), 6.46 (dd, *J* = 2.7, 8.5, 1 H), 3.20 (t, *J* = 7.5, 4 H), 2.44 (s, 2 H), 1.60 (q, *J* = 7.4, 4 H), 1.31 (s, 6 H), 0.93 (t, *J* = 7.4, 6 H).

EXAMPLE 235

3,4-Dihydro-4,4-dimethyl-6-propylamino-2(1*H*)-quinolinone (Compound 499, Structure 52 of Scheme IX, where $R^1 = R^2 =$ methyl, $R^4 =$ propyl, $R^5 =$ H, W = carbon)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **495** (Structure **51** of Scheme IX, where $R^1 = R^2 =$ methyl, W = carbon) in place of Compound **200**. Compound **499** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) 7.83 (br s, 1 H), 6.59(d, *J* = 8.4, 1 H), 6.54 (d, *J* = 2.4, 1 H), 6.41 (dd, *J* = 2.4, 8.4, 1 H), 3.56 (br s, 1 H), 3.04 (t, *J* = 7.1, 2 H), 2.47 (s, 2 H), 1.61 (q, *J* = 7.4, 4 H), 1.27 (s, 6 H), 0.97 (t, *J* = 7.4, 6 H).

EXAMPLE 236

3,4-Dihydro-4,4-dimethyl-6-(N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound 500, Structure 52 of Scheme IX, where $R^1 = R^2 =$ methyl, $R^4 =$ trifluoroethyl, $R^5 =$ H, W = carbon)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **495** (Structure **51** of Scheme IX, where $R^1 = R^2 =$ methyl, W = carbon) and trifluoroacetaldehyde in place of Compound **200** and propionaldehyde. Compound **500** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.12 (brs, 1 H), 6.64 (m, 2 H), 6.51 (dd, *J* = 2.5, 8.4, 1 H), 3.85 (br s, 1 H), 3.74 (m, 2 H), 2.44 (s, 2 H), 1.30 (s, 6 H).

EXAMPLE 237

3,4-Dihydro-4,4-dimethyl-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound 501, Structure 52 of Scheme IX, where $R^1 = R^2 =$ methyl, $R^4 = R^5 =$ trifluoroethyl, W = carbon)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using Compound **495** (Structure **51** of Scheme IX, where $R^1 = R^2 =$ methyl, W = carbon) and trifluoroacetaldehyde in place of Compound **200** and paraformaldehyde. Compound **501** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.17 (brs, 1 H), 6.88 (d, *J* = 2.6, 1 H), 6.76 (dd, *J* = 2.5, 8.6, 1 H), 6.72 (d, *J* = 8.6, 1 H), 3.98 (q, *J* = 8.6, 4 H), 2.48 (s, 2 H), 1.31 (s, 6 H).

EXAMPLE 238

3,4-Dihydro-6-(N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound 502, Structure 52 of Scheme IX, where $R^1 = R^2 = R^5 = H$, R^4 = trifluoroethyl, W = carbon)

6-Amino-3,4-dihydro-2(1*H*)-quinolinone (Compound **503**, Structure **51** of Scheme IX, where $R^1 = R^2 = H$, W = carbon):

To a solution of 3,4-dihdyro-2(1*H*)-quinolinone (Compound **504**, Structure **49** of Scheme IX, where $R^1 = R^2 = H$, W = carbon) (1 g, 6.8 mmol) and conc. Sulfuric acid (15 mL) was added fuming nitric acid (0.3 mL in 3 mL of conc. Sulfuric acid). Stirred at 0 oC for 30 min. then cast into ice to give a yellow precipitate. Filtered, washed with water and dried to afford 1.3 g (100%) of as a white crystalline solid. A solution of the above solid (200 mg, 1.04 mmol) and DCM (30 mL) was hydrogenated over 10% Pd/C (20 mg) at 1 atm and rt. After 15 hrs. filtered through Celite and concentrated in vacuo to afford 168 mg (100%) of Compound **503** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.42 (brs, 1 H), 6.53 (m, 3 H), 3.52 (brs, 2 H), 2.87 (t, *J* = 7.1, 2 H), 2.58 (t, *J* = 7.1, 2 H).

3,4-Dihydro-6-(N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **502**, Structure **52** of Scheme IX, where $R^1 = R^2 = R^5 = H$, R^4 = trifluoroethyl, W = carbon):

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **503** and trifluoroacetaldehyde in place of Compound **200** and propionaldehyde. Compound **502** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.79 (brs, 1 H), 6.62 (d, *J* = 8.5, 1 H), 6.51 (m, 2 H), 3.74 (q, *J* = 8.9, 2 H), 2.90 (t, *J* = 7.2, 2 H), 2.59 (t, *J* = 7.2, 2 H).

EXAMPLE 239

3,4-Dihydro-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound 505, Structure 52 of Scheme IX, where $R^1 = R^2 = H$, $R^4 = R^5$ = trifluoroethyl, W = carbon)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using Compound **503** and trifluoroacetaldehyde in place of Compound **200** and paraformaldehyde. Compound **505** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.86 (brs, 1 H), 6.76 (m, 2 H), 6.68 (d, *J* = 8.5, 1 H), 3.98 (q, *J* = 8.6, 4 H), 2.94 (t, *J* = 7.1, 2 H), 2.62 (t, *J* = 7.1, 2 H).

EXAMPLE 240

5-(bis-N,N-2,2,2-Trifluoroethyl)amino-3,3-spirocyclohexyl-2-indolone

(Compound 506, Structure 55 of Scheme X, where $R^1 = R^2$ = trifluoroethyl)

5-Amino-3-spirocyclohexyloxindole (Compound **507**, Structure **54** of Scheme X):

This compound was prepared in a similar fashion as that described in Example 1, General Procedures II and III but using 3-spirocyclohexyloxindole in place of Compound **202**. Compound **507** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.74 (bs, 1H), 6.86 (d, J = 1.9, 1H), 6.69 (d, J = 7.9, 1H), 6.55 (dd, J = 2.2, 8.1, 1H), 3.54 (bs, 2H), 1.93-1.76 (mm, 4H), 1.73-1.57 (mm, 6H).

5-(bis-N,N-2,2,2-Trifluoroethyl)amino-3,3-spirocyclohexyl-2-indolone (Compound **506**, Structure **55** of Scheme X, where $R^1 = R^2$ = trifluoroethyl):

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using Compound **507** and trifluoroacetaldehyde in place of Compound **200** and paraformaldehyde. Compound **506** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.52 (bs, 1H), 7.11 (s, 1H), 6.84 (s, 2H), 3.95 (q, J = 8.7, 4H), 1.97-1.92 (m, 2H), 1.89-1.83 (m, 2H), 1.71-1.57 (m, 6H).

EXAMPLE 241

7-(bis-N,N-2,2,2-Trifluoroethyl)amino-1,4-benzoxazin-3(4*H*)-one

(Compound 508, Structure 57 of Scheme X, where $R^1 = R^2$ = trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 7-amino-1,4-benzoxazin-3(4*H*)-one (Compound **509**, Structure **56** of Scheme X) and trifluoroacetic acid as white solid. ^{1}H NMR (500 MHz, $CDCl_3$) 8.12 (bs, 1H), 6.72 (d, J = 8.8, 1H), 6.59 (d, J = 2.9, 1H), 6.53 (dd, J = 8.8, 2.9, 1H), 4.61 (s, 2H), 3.97 (q, $J_{H\text{-}F}$ = 8.8, 4H).

EXAMPLE 242

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-2,4-dichloroquinoline

(Compound 510, Structure 59 of Scheme X, where $R^1 = R^2$ = trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 6-amino-1,4-dichloro-2(1H)-quinolinone (Compound **511**, Structure **58** of

Scheme X) and trifluoroacetic acid as brown solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 7.99 (dd, J = 1.0, 8.8, 1H), 7.47-7.50 (m, 3H), 4.22, J = 8.8, 4H).

EXAMPLE 243

7-Amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 512, Structure 61 of Scheme XI, where R = R^1 = H)

A solution of 1,3-phenylenediamine (5.4 g, 50 mmol) and ethyl 4,4,4-trifluoroacetoacetate (11 g, 60 mmol) in ethanol (100 mL) was heated at reflux overnight to give rise to a yellow slurry. P-Toluenesulfonic acid monohydrate (0.19 g, 1.0 mmol) was added and the reaction mixture was allowed to stir at reflux for additional 24 h. The reaction was cooled to room temperature to generate a large amount of solid. Filtration of the solid followed by washing the solid with methanol (2 x 10 mL) afforded Compound **512** as a yellowish solid (8.5 g, 75%): ^{1}H NMR (400 MHz, acetone-d_6) 10.91 (bs, 1 H), 7.47 (dq, J = 6.7, 2.4, 1 H), 6.70 (dd, J = 6.7, 2.2, 1 H), 6.65 (d, J = 2.2, 1 H), 6.50 (s, 1 H), 5.65 (bs, 2 H).

EXAMPLE 244

7-Propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 513, Structure 62 of Scheme XI, where R = R^1 = R^2 = H, R^3 = propyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **512** (Structure **61** of Scheme XI, where R^1 = R = H) (100 mg, 0.45 mmol) in place of Compound **200**. Compound **513** was isolated in 84% as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.62 (bs, 1 H), 7.46 (dq, J = 9.0, 1.5, 1 H), 6.68 (dd, J = 9.0, 2.1, 1 H), 6.57 (d, J = 2.1, 1 H), 6.48 (s, 1 H), 5.99 (bs, 1 H), 3.17 (m, 1 H), 1.68 (hex, J = 7.8, 2 H), 1.01 (t, J = 7.8, 3 H).

EXAMPLE 245

7-Isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 514, Structure 62 of Scheme XI, where R = R^1 = R^2 = H, R^3 = isopropyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **512** (Structure **61** of Scheme XI, where R^1 = R = H) (10 mg, 0.045 mmol) and acetone (58 mg, 1.0 mmol) in place of Compound **200** and propionaldehyde.

Compound **514** was isolated in 66% as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 10.70 (bs, 1 H), 7.58 (dq, J = 9.0, 1.8, 1 H), 6.70 (s, 1 H), 6.51 (dd, J = 9.0, 2.3, 1 H), 6.31 (d, J = 2.3, 1 H), 4.12 (d, J = 6.0, 1 H), 3.73 (m, 1 H), 1.26 (d, J = 6.2, 6 H).

EXAMPLE 246

7-(2,2-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **515**, Structure **62** of Scheme XI, where R = R^1 = R^2 = H, R^3 = 2,2-dimethylpropyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **512** (Structure **61** of Scheme XI, where R^1 = R = H) (10 mg, 0.045 mmol) and trimethylacetylaldehyde (86 mg, 1.0 mmol) in place of Compound **200** and propionaldehyde. Compound **515** was isolated in 60% as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.55 (bs, 1 H), 7.56 (dq, J = 9.0, 1.8, 1 H), 6.71 (s, 1 H), 6.58 (dd, J = 9.1, 2.3, 1 H), 6.42 (d, J = 2.3, 1 H), 4.30 (t, J = 6.0, 1 H), 3.00 (d, J = 6.0, 1 H), 1.02 (s, 3 H).

EXAMPLE 247

7-(2-Methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **516**, Structure **62** of Scheme XI, where R = R^1 = R^2 = H, R^3 = 2-methylpropyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **512** (Structure **61** of Scheme XI, where R^1 = R = H) (10 mg, 0.045 mmol) and isobutyraldehyde (72 mg, 1.0 mmol) in place of Compound **200** and propionaldehyde. Compound **516** was isolated in 67% as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.43 (bs, 1 H), 7.57 (dq, J = 9.0, 1.8, 1 H), 6.70 (s, 1 H), 6.55 (dd, J = 9.1, 2.4, 1 H), 6.38 (d, J = 2.4, 1 H), 4.34 (t, J = 6.2, 1 H), 3.04 (t, J = 6.3, 1 H), 1.01 (d, J = 6.4, 6 H).

EXAMPLE 248

7-Methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **517**, Structure **62** of Scheme XI, where R = R^1 = R^2 = H, R^3 = methyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **512** (Structure **61** of Scheme XI, where R^1 = R = H) (10 mg, 0.045 mmol) and paraformaldehyde (10 mg, 0.33 mmol) in place of Compound **200** and propionaldehyde. Compound **517** was isolated in 73% as a yellow solid: ^{1}H NMR (400 MHz,

acetone-d_6) 10.68 (bs, 1 H), 7.46 (dq, J = 9.0, 1.5, 1 H), 6.66 (dd, J = 9.0, 2.1, 1 H), 6.52 (d, J = 2.1, 1 H), 6.47 (s, 1 H), 5.99 (bs, 1 H), 2.88 (d, J = 5.0, 3 H).

EXAMPLE 249

7-Dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 518, Structure 62 of Scheme XI, where R = R^1 = H, R^3 = R^2 = methyl)

This compound was prepared in a similar fashion as that described in Example 15, General Procedure VIII but using Compound **512** (Structure **61** of Scheme XI, where R^1 = R = H) (10 mg, 0.045 mmol) in place of Compound **200**. Compound **518** was isolated in 50% as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.22 (bs, 1 H), 7.63 (dq, J = 9.0, 1.5, 1 H), 6.72 (s, 1 H), 6.71 (dd, J = 9.0, 2.1, 1 H), 6.43 (d, J = 2.1, 1 H), 3.10 (s, 6 H).

EXAMPLE 250

7-Benzylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 519, Structure 62 of Scheme XI, where R = R^1 = R^2 = H, R^3 = benzyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **512** (Structure **61** of Scheme XI, where R^1 = R = H) and benzaldehyde in place of Compound **200** and propionaldehyde. Compound **519** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.96 (bs, 1 H), 7.49 (dq, J= 9.0, 1.5, 1 H), 7.41 (d, J = 7.6, 2 H), 7.33 (t, J = 7.6, 3 H), 7.27 (t, J = 7.6, 1 H), 6.76 (dd, J = 9.0, 2.1, 1 H), 6.60 (d, J = 2.1, 1 H), 4.45 (d, J = 5.9, 2 H).

EXAMPLE 251

7-(2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 520, Structure 62 of Scheme XI, where R = R^1 = R^2 = H, R^3 = 2,2,3,3,3-Pentafluoropropyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **512** (Structure **61** of Scheme XI, where R^1 = R = H) (100 mg, 0.45 mmol) and pentafluoropropionic acid in place of Compound **200** and 2,2-difluoroacetic acid. Compound **520** was isolated in 50% as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.88 (bs, 1 H), 7.58 (dq, J = 9.0, 1.5, 1 H), 6.87 (dd, J = 9.0, 2.1, 1 H), 6.81 (d, J = 2.1, 1 H), 6.58 (s, 1 H), 6.47 (bs, 1 H), 4.14 (td, J = 15.5, 6.5, 2 H).

EXAMPLE 252

7-Butylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **521**, Structure **62** of Scheme XI, where R = R^1 = R^2 = H, R^3 = butyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **512** (Structure **61** of Scheme XI, where R^1 = R = H) (10 mg, 0.045 mmol) and butyraldehyde in place of Compound **200** and propionaldehyde. Compound **521** was isolated in 80% as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.40 (bs, 1 H), 7.58 (dq, *J* = 9.0, 1.5, 1 H), 6.72 (s, 1 H), 6.58 (dd, *J* = 9.0, 2.1, 1 H), 6.39 (d, *J* = 2.1, 1 H), 4.23 (t, *J* = 6.0, 1 H), 3.22 (q, *J* = 6.5, 2 H), 1.69-1.42 (m, 4 H), 1.0 (t, *J* = 7.3, 3 H).

EXAMPLE 253

7-Ethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **522**, Structure **62** of Scheme XI, where R = R^1 = R^2 = H, R^3 = ethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **512** (Structure **61** of Scheme XI, where R^1 = R = H) (100 mg, 0.45 mmol) and acetic acid in place of Compound **200** and 2,2-difluoroacetic acid. Compound **522** was isolated in 89% as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.78 (bs, 1 H), 7.56 (dq, *J* = 9.0, 1.5, 1 H), 6.76 (dd, *J* = 9.0, 2.1, 1 H), 6.65 (d, *J* = 2.1, 1 H), 6.57 (s, 1 H), 6.02 (bs, 1 H), 3.32 (m, 2 H), 1.36 (t, *J* = 7.3, 3 H).

EXAMPLE 254

7-(N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **523**, Structure **62** of Scheme XI, where R = R^1 = R^2 = H, R^3 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **512** (Structure **61** of Scheme XI, where R^1 = R = H) (100 mg, 0.45 mmol) and trifluoroacetic acid in place of Compound **200** and 2,2-difluoroacetic acid. Compound **523** was isolated in 50% as a yellow solid: mp 238-239 °C; ^{1}H NMR (400 MHz, acetone-*d*$_6$) 10.95 (bs, 1 H), 7.56 (dq, *J* = 9.0, 1.5, 1 H), 6.86 (dd, *J* = 9.0, 2.1, 1 H), 6.80 (d, *J* = 2.1, 1 H), 6.60 (s, 1 H), 6.50 (bs, 1 H), 4.05 (m, 2 H).

EXAMPLE 255

7-Cyclohexylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 524, Structure 62 of Scheme XI, where $R = R^1 = R^2 = H$, R^3 = cyclohexyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **512** (Structure **61** of Scheme XI, where $R^1 = R = H$) and cyclohexanone in place of Compound **200** and propionaldehyde. Compound **524** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 10.6 (bs,1 H), 7.44 (dd, J = 9.3, 2.4, 1 H), 6.67 (dd, J = 9.3, 2.4, 1 H), 6.59 (d, J = 2.4, 1 H), 6.46 (s, 1 H), 5.84 (d, J = 7.3, 1 H), 3.39-3.31 (m, 1 H), 1.81-1.77 (m, 2 H), 1.68-1.64 (m, 1 H), 1.46-1.38 (m, 2 H), 1.32-1.22 (m, 3 H).

EXAMPLE 256

7-Cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 525, Structure 62 of Scheme XI, where $R = R^1 = R^2 = H$, R^3 = cyclopentyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **512** (Structure **61** of Scheme XI, where $R^1 = R = H$) and cyclopentanone in place of Compound **200** and propionaldehyde. Compound **525** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 10.8 (bs, 1 H), 7.45 (dd, J = 8.8, 2.2, 1 H), 6.67 (dd, J = 8.8, 2.4, 1 H), 6.59 (d, J = 2.4, 1 H), 6.48 (s, 1 H), 5.98 (d, J = 5.9, 1 H), 3.90-3.84 (m, 1 H), 2.09-2.04 (m, 2 H), 1.79-1.71 (m, 2 H), 1.68-1.55 (m, 4 H).

EXAMPLE 257

7-Cyclobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 526, Structure 62 of Scheme XI, where $R = R^1 = R^2 = H$, R^3 = cyclobutyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **512** (Structure **61** of Scheme XI, where $R^1 = R = H$) and cyclobutanone in place of Compound **200** and propionaldehyde. Compound **526** was isolated as a yellow solid: ^{1}H NMR (500 MHz, DMSO-d_6) 11.8 (bs, 1H), 7.36 (d, J = 9.3, 1 H), 6.98 (d, J = 5.9, 1 H), 6.55 (dd, J = 9.3, 1.5, 1 H), 6.43 (s, 1 H), 6.34 (d, J = 1.5, 1 H), 3.85-3.80 (m, 1 H), 2.37-2.32 (m, 2 H), 1.89-1.83 (m, 2 H), 1.78-1.72 (m, 2 H).

EXAMPLE 258

7-(2-Hydroxy-2-methylpropionyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 527, Structure 62 of Scheme XI, where $R = R^1 = R^2 = H$, R^3 = 2-hydroxy-2-methylpropionyl)

To a solution of Compound **512** (Structure **61** of Scheme XI, where $R^1 = R = H$) (12 mg, 0.036 mmol) in THF (2 mL) was added 1-chlorocarbonyl-1-methylethyl acetate (10 mg, 0.06 mmol), the mixture was stirred at room temperature for a few minutes. Triethylamine (10 mg, 0.10 mmol) was added and the reaction was stirred for additional 2 h and then was quenched with 5% NaOH. The mixture was extracted with EtOAc (2x 20 mL), washed with brine, and concentrated. Chromatography afforded Compound **527** as a white solid: mp 289-291 °C; ^1H NMR (400 MHz, $ODCD_3$) 8.14 (d, J = 2.0, 1 H), 7.75 (dq, J = 8.9, 2.0, 1 H), 7.42 (dd, J = 8.9, 2.1, 1 H), 6.88 (s, 1 H), 4.85 (s, 6 H).

EXAMPLE 259

7-(Trifluoroacetamido)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 528, Structure 62 of Scheme XI, where $R = R^1 = R^2 = H$, R^3 = trifluoroacetyl)

To a solution of Compound **512** (Structure **61** of Scheme XI, where $R^1 = R = H$) (46 mg, 0.20 mmol) in 1 mL pyridine was added trifluoroacetic anhydride (0.14 mL, 1.0 mmol). After 16 h, the solution was partitioned between EtOAc (30 mL) and 1N $NaHSO_4$ (30 mL). The organic layer was washed sequentially with pH 6.88 phosphate buffer (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered and concentrated. Flash chromatography (9:1 CH_2Cl_2:MeOH) afforded 54 mg (83%) of Compound **528**: R_f 0.24 (9:1 CH_2Cl_2:MeOH); ^1H NMR (400 MHz, acetone-d_6) 11.3 (broad s, 1 H), 10.7 (broad s, 1 H), 8.41 (d, J = 1.7, 1 H), 7.81 (d, J = 8.9, 1 H), 7.58 (dd, J = 9.0, 1.8, 1 H), 6.92 (s, 1 H).

EXAMPLE 260

1-Methyl-7-methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 529, Structure 63 of Scheme XI, where $R = R^1 = R^2 = H$, $R^3 = R^4$ = methyl)

This compound was prepared in a similar fashion as that described in Example 92, General Procedure X from Compound **517** (Structure **62** of Scheme XI, where $R = R^1 = R^2 = H$, R^3 = methyl). Compound **529** was isolated as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) 7.63

(dq, J = 9.0, 1.5, 1 H), 6.78 (s, 1 H), 6.57 (dd, J = 9.0, 2.1, 1 H), 6.37 (d, J = 2.1, 1 H), 4.42 (bs, 1 H), 3.69 (s, 3 H), 2.97 (d, J = 5.2, 3 H).

EXAMPLE 261

1-Methyl-7-dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 530, Structure 63 of Scheme XI, where R = R^1 = H, R^2 = R^3 = R^4 = methyl)

This compound was prepared in a similar fashion as that described in Example 92, General Procedure X from Compound **518** (Structure **62** of Scheme XI, where R = R^1 = H, R^3 = R^2 = methyl). Compound **530** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.66 (dq, J = 9.0, 1.5, 1 H), 6.78 (s, 1 H), 6.72 (dd, J = 9.0, 2.1, 1 H), 6.39 (d, J = 2.1, 1 H), 3.70 (s, 3 H), 3.13 (s, 6 H).

EXAMPLE 262

1-Methyl-7-(N-methyl-N-isopropylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 531, Structure 63 of Scheme XI, where R = R^1 = H, R^2 = R^4 = methyl, R^3 = isopropyl)

This compound was prepared in a similar fashion as that described in Example 92, General Procedure X from Compound **514** (Structure **62** of Scheme XI, where R = R^1 = R^2 = H, R^3 = isopropyl). Compound **531** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) 7.65 (dd, J = 9.3, 2.4, 1 H), 6.79 (dd, J = 9.3, 2.4, 1 H), 6.77 (s, 1 H), 6.47 (d, J = 2.4, 1 H), 4.27-4.23 (m, 1 H) 3.70 (s, 3 H), 2.89 (s, 3 H), 1.26 (d, J = 6.3, 6 H).

EXAMPLE 263

1-Methyl-7-(2,2,2-trifluoromethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 532, Structure 63 of Scheme XI, where R = R^1 = R^2 =H, R^4 = methyl, R^3 = trifluoromethyl)

This compound was prepared in a similar fashion as that described in Example 92, General Procedure X from Compound **523** (Structure **62** of Scheme XI, where R = R^1 = R^2 = H, R^3 = 2,2,2-trifluoroethyl). Compound **532** was isolated as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$ + DMSO-d_6) 7.64 (dd, J = 8.8, 2.0, 1 H), 6.84 (s, 1 H), 6.71 (dd, J = 8.8, 2.0, 1 H), 6.62 (d, J = 2.0, 1 H), 5.96 (bt, J = 6.8, 1 H), 3.93-3.86 (m, 2 H), 3.68 (s, 3 H).

EXAMPLE 264

3-Fluoro-7-(2,2,2-trifluoromethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 533, Structure 62 of Scheme XI, where R = fluoro, $R^1 = R^2 = H$, R^3 = trifluoromethyl)

3-Fluoro-7-amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **534**, Structure **61** of Scheme XI, where R = fluoro, $R^1 = H$):

This compound was prepared in a similar manner as that described in Example 1, General Procedures I, II and III but using ethyl 2,4,4,4-tetrafluoroacetoacetate hydrate in place of ethyl 4,4,4-trifluoroacetoacetate. Compound **534** was isolated as a white solid: ^{1}H NMR (500 MHz, DMSO-d_6) 12.4 (bs, 1 H), 7.39 (dd, J = 8.8, 2.0, 1 H), 6.64 (dd, J = 9.3, 1.9, 1 H), 6.50 (d, J = 2.4, 1 H), 6.05 (bs, 2 H).

3-Fluoro-7-(2,2,2-trifluoromethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **533**, Structure **62** of Scheme XI, where R = fluoro, $R^1 = R^2 = H$, R^3 = trifluoromethyl):

Compound **534** was dissolved in trifluoroacetic acid (15 mL) and heated to 60 ° C for 2 h, cooled to room temperature where sodium borohydride (350 mg, 9.25 mmol, 5.0 equiv) was carefully added in portions to the reaction mixture. After complete addition of sodium borohydride the reaction mixture was allowed to stir for 16 h, poured over ice and neutralized to pH 7 with NaOH pellets. A white precipitate was filtered from the aqueous solution, redissolved in EtOAc (200 mL), washed with water (25 mL), brine (25 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield an off white solid. Purification by re-crystallization (MeOH) afforded 135 mg (22%) of Compound **533** as a white solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.18 (bs, 1 H), 7.58 (dd, J = 8.9,2.1, 1 H), 6.90 (dd, J = 9.0, 2.2, 1 H), 6.81 (d, J = 2.3, 1 H), 6.40 (bm, 1 H), 4.04 (m, 2 H).

EXAMPLE 265

3-Fluoro-7-isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 535, Structure 62 of Scheme XI, where R = fluoro, $R^1 = R^2 = H$, R^3 = isopropyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **534** (Structure **61** of Scheme XI, where $R^1 = H$, R = fluoro) and acetone in place of Compound **200** and propionaldehyde. Compound **535** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 11.0 (bs, 1H), 7.49 (d, J = 9.1, 1 H), 6.72 (d, J =

9.1, 1 H), 6.59 (t, J = 2.4, 1 H), 6.86 (s, 1 H), 5.69 (bs, 1 H), 3.71-3.67 (m, 1 H) , 1.24 (d, J = 6.3, 6 H).

EXAMPLE 266

3-Fluoro-7-cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 536, Structure 62 of Scheme XI, where R = fluoro, $R^1 = R^2 = H$, R^3 = cyclopentyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **534** (Structure **61** of Scheme XI, where R^1 = H, R = fluoro) and cyclopentanone in place of Compound **200** and propionaldehyde. Compound **536** was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 11.1 (bs, 1 H), 7.49 (dd, J = 9.3, 2.4, 1 H), 6.73 (dd, J = 9.3, 2.4, 1 H), 6.61 (d, J = 2.4, 1 H), 5.88 (bs, 1 H), 3.87-3.83 (m, 1 H), 2.08-1.98 (m, 2 H), 1.76-1.56 (m, 6 H).

EXAMPLE 267

3-Fluoro-7-cyclohexylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 537, Structure 62 of Scheme XI, where R = fluoro, $R^1 = R^2 = H$, R^3 = cyclohexyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **534** (Structure **61** of Scheme XI, where R^1 = H, R = fluoro) and cyclocyclohexanone in place of Compound **200** and propionaldehyde. Compound **537** was isolated as a yellow solid: ^{1}H NMR (500, acetone-d_6) 11.1 (bs, 1 H), 7.48 (dd, J = 9.3, 2.4, 1 H), 6.73 (dd, J = 9.3, 2.4, 1 H), 6.61 (d, J = 2.4, 1 H), 5.74 (d, J = 7.3, 1 H), 3.36-3.31 (m, 1 H), 1.81-1.77 (m, 2 H), 1.67-1.64 (m, 1 H), 1.43-1.37 (m, 2 H), 1.31-1.21 (m, 3 H).

EXAMPLE 268

3-Fluoro-7-cyclobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 538, Structure 62 of Scheme XI, where R = fluoro, $R^1 = R^2 = H$, R^3 = cyclobutyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **534** (Structure **61** of Scheme XI, where R^1 = H, R = fluoro) and cyclocyclobutanone in place of Compound **200** and propionaldehyde. Compound **538** was isolated as a yellow solid: ^{1}H NMR (500, acetone-d_6) 12.3 (bs, 1 H), 7.41 (dd, J = 8.8, 2.4, 1 H), 6.88 (d, J = 5.9, 1 H), 6.63 (dd, J = 8.8, 2.4, 1 H), 6.37 (d, J = 2.4, 1 H), 3.84-3.80 (m, 1 H), 2.38-2.32 (m, 2 H), 1.91-1.83 (m, 2 H), 1.80-1.72 (m, 2 H).

EXAMPLE 269

3-Fluoro-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 539, Structure **62** of Scheme XI, where R = fluoro, $R^1 = R^2$ = H, R^3 = propyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **534** (Structure **61** of Scheme XI, where R^1 = H, R = fluoro) in place of Compound **200**. Compound **539** was isolated as a yellow solid: ^{1}H NMR (500, acetone-d_6) 11.0 (bs, 1 H), 7.50 (dd, *J* = 8.8, 2.2, 1 H), 6.75 (dd, *J* = 8.8, 2.2, 1 H), 6.58 (d, *J* = 2.4, 1 H), 5.89 (bs, 1 H), 3.18-3.14 (m, 2 H), 1.70-1.65 (m, 2 H) , 0.99 (t, *J* = 7.3, 3 H).

EXAMPLE 270

3-Fluoro-1-methyl-7-(N-methyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **540**, Structure **63** of Scheme XI, where R = fluoro, R^1 = H, $R^2 = R^4$ = methyl, R^3 = isopropyl)

This compound was prepared in a similar fashion as that described in Example 92, General Procedure X from Compound **535** (Structure **62** of Scheme XI, where R = fluoro, $R^1 = R^2$ = H, R^3 = isopropyl). Compound **540**was isolated as a yellow solid: ^{1}H NMR (500 MHz, acetone-d_6) 7.69 (dd, *J* = 9.3, 2.4, 1 H), 6.94 (dd, *J* = 9.3, 2.4, 1 H), 6.67 (d, *J* = 2.4, 1 H), 4.43-4.37 (m, 1 H), 3.94 (s, 3 H), 3.71 (s, 3 H), 1.23 (d, *J* = 6.3, 6 H).

EXAMPLE 271

3-Fluoro-1-methyl-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **541**, Structure **63** of Scheme XI, where R = fluoro, $R^1 = R^2$ = H, R^4 = methyl, R^3 = propyl)

This compound was prepared in a similar fashion as that described in Example 92, General Procedure X from Compound **539** (Structure **62** of Scheme XI, where R = fluoro, $R^1 = R^2$ = H, R^3 = propyl). Compound **541** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.63 (dd, *J* = 9.1, 1.9, 1 H), 6.62 (dd, *J* = 9.1, 2.1, 1 H), 6.38 (d, *J* = 2.1, 1 H), 4.23 (bs, 1 H), 3.23 (s, 3 H), 3.19 (t, *J* = 7.1, 6 H), 1.75-1.67 (m, 2 H), 1.05 (t, *J* = 7.4, 3 H).

EXAMPLE 272

6-Fluoro-7-amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 542, Structure 63 of Scheme XI, where R^1 = fluoro, R = H)

This compound was prepared in a similar manner as that described in Example 243 but using 4-fluoro-1,3-phenylenediamine (Structure **60** of Scheme XI, where R^1 = fluorine) in place of 1,3-phenylenediamine. Compound **542** was isolated as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) 7.35 (d, *J* = 9.2, 1 H), 6.71 (d, *J* = 7.5, 1 H), 6.65 (s, 1 H).

EXAMPLE 273

6-Fluoro-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 543, Structure 62 of Scheme XI, where R^1 = fluoro, R = R^2 = H, R^3 = propyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **542** (Structure **61** of Scheme XI, where R^1 = fluoro, R = H) in place of Compound **200**. Compound **543** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.49 (d, *J* = 7.5, 1 H), 6.78 (s, 1 H), 6.40 (d, *J* = 7.5, 1 H), 4.51 (br t, 1 H), 3.22 (m, 2 H), 1.74 (q, *J* = 7.3, 2 H), 1.07 (t, *J* = 7.3, 3 H).

EXAMPLE 274

6-Fluoro-7-isobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 544, Structure 62 of Scheme XI, where R^1 = fluoro, R = R^2 = H, R^3 = isobutyl)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **542** (Structure **61** of Scheme XI, where R^1 = fluoro, R = H) and isobutyraldehyde in place of Compound **200** and propionaldehyde. Compound **544** was isolated as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) 7.30 (d, *J* = 7.5, 1 H), 6.61 (s, 1 H), 6.59 (d, *J* = 7.5, 1 H), 3.05 (d, *J* = 7.3, 2 H), 2.00 (m, 1 H), 1.00 (d, *J* = 6.6, 6 H).

EXAMPLE 275

6-Fluoro-1-methyl-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 545, Structure 63 of Scheme XI, where R^1 = fluoro, R = R^2 = H, R^4 = methyl, R^3 = propyl)

This compound was prepared in a similar fashion as that described in Example 92, General Procedure X from Compound **543** (Structure **62** of Scheme XI, where R^1 = fluoro, R =

R^2 = H, R^3 = propyl). Compound **545** was isolated as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) 7.34 (d, J = 9.2, 1 H), 6.73 (s, 1 H), 6.66 (d, J = 7.6, 1 H), 3.74 (s, 3 H), 3.31 (m under solvent peak, 2 H), 1.75 (m, 2 H), 1.05 (t, J = 7.4, 3 H).

EXAMPLE 276

6-Fluoro-1-methyl-7-(N-methyl-N-propylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **546**, Structure **63** of Scheme XI, where R^1 = fluoro, R = H, R^2 = R^4 = methyl, R^3 = propyl)

This compound was prepared in a similar fashion as that described in Example 92, General Procedure X from Compound **543** (Structure **62** of Scheme XI, where R^1 = fluoro, R = R^2 = H, R^3 = propyl). Compound **546** was isolated as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) 7.39 (d, J = 15.3, 1 H), 6.79 (s under d, 2 H), 3.75 (s, 3 H), 3.43 (m, 2 H), 3.10 (s, 3 H), 1.70 (m, 2 H), 0.95 (t, J = 7.4, 3 H).

EXAMPLE 277

7-Amino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **547**, Structure **61** of Scheme XI, where R^1 = methyl, R = H)

This compound was prepared in a similar manner as that described in Example 243 but using 2,4-diaminotoluene (Structure **60** of Scheme XI, where R^1 = methyl) in place of 1,3-phenylenediamine. Compound **547** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 11.00 (br s, 1 H), 7.21 (s, 1 H), 6.54 (s, 1 H), 6.45 (s, 1 H), 2.10 (s, 3 H).

EXAMPLE 278

7-Isobutylamino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **548**, Structure **62** of Scheme XI, where R^1 = methyl, R^2 = isobutyl, R = R^3 = H)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **547** (Structure **61** of Scheme XI, where R^1 = methyl, R = H) and isobutyraldehyde in place of Compound **200** and propionaldehyde. Compound **548** was isolated as a yellow solid: ^{1}H NMR (400 MHz, DMSO-d_6) 11.00 (br s, 1 H), 7.22 (s, 1 H), 6.45 (s, 1 H), 6.40 (s, 1 H), 6.05 (br t, 1 H), 2.92 (m, 2 H), 2.15 (s, 3 H), 1.99 (m, 1 H), 0.93 (d, J = 6.6, 6 H).

EXAMPLE 279

7-Propylamino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 549, Structure 62 of Scheme XI, where R^1 = methyl, R^2 = propyl, R = R^3 = H)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **547** (Structure **61** of Scheme XI, where R^1 = methyl, R = H) in place of Compound **200**. Compound **549** was isolated as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) 10.60 (br s, 1 H), 7.42 (s, 1 H), 6.70 (s, 1 H), 6.33 (s, 1 H), 4.05 (br t, 1 H), 3.20 (m, 2 H), 2.20 (s, 3 H), 1.74 (q, J = 7.4, 2 H), 1.06 (t, J = 7.4, 3 H).

EXAMPLE 280

7-(1,1-Dimethyl-3-oxobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 550, Structure 64 of Scheme XII)

A solution of Compound **512** (Structure **61a** of Scheme XII) (460 mg, 2.0 mmol) and a catalytic amount of acetic acid in acetone (5 mL) was stirred at room temperature overnight. Removal of solvent and chromatography of the reaction mixture afforded Compound **550** (100 mg, 15%) as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) 11.03 (bs, 1 H), 7.57 (dq, J = 9.0, 1.8, 1 H), 6.73 (d, J = 2.1, 1 H), 6.72 (s, 1 H), 6.62 (dd, J = 9.0, 2.1, 1 H), 4.90 (bs, 1 H), 2.89 (s, 2 H), 2.14 (s, 3 H), 1.52 (s, 6 H).

EXAMPLE 281

7-(1,1,3-Trimethyl-3-hydroxybutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 551, Structure 65 of Scheme XII)

To a solution of Compound **550** (Structure **61a** of Scheme XII) (10 mg, 0.031 mmol) in THF at –78 °C was added MeLi (0.1 mL, 1.4 M in ether) and resulting mixture was stirred for 30 min. and quenched with water. Extraction with EtOAc followed by chromatography afforded Compound **551** (5.0 mg, 49%) as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) 11.40 (bs, 1 H), 7.53 (dq, J = 9.0, 1.8, 1 H), 6.71 (d, J = 2.1, 1 H), 6.70 (s, 1 H), 6.60 (dd, J = 9.0, 2.1, 1 H), 5.50 (bs, 1 H), 2.18 (s, 1 H), 1.97 (s, 2 H), 1.55 (s, 6 H), 1.38 (s, 6 H).

EXAMPLE 282

7-(1,1,3-Trimethyl-3-butenylamino)-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **552**, Structure **66** of Scheme XII)

A solution of Compound **551** (Structure **65** of Scheme XII) (7.0 mg, 0.020 mmol) in acetone was treated with catalytic amount of acetic acid at room temperature overnight and standard work-up provided Compound **552** (2.7 mg, 41%) as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.30 (bs, 1 H), 7.61 (dq, J = 8.8, 1.5, 1 H), 6.85 (d, J = 2.1, 1 H), 6.85 (s, 1 H), 6.75 (dd, J = 8.8, 2.1, 1 H), 5.21 (s, 1 H), 4.39 (s, 1 H), 2.73 (d, J = 15.4, 1 H), 2.17 (d, J = 15.4, 1 H), 1.78 (s, 3 H), 1.68 (s, 3 H), 1.50 (s, 3 H).

EXAMPLE 283

7-(1-Phenylaminocarbonylisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **553**, Structure **69** of Scheme XIII)

7-amino-2-ethoxy-4-trifluoromethylquinoline (Compound **554**, Structure **67** of Scheme XIII):

This compound was prepared in a similar method as that described in Example 243. A solution of 1,3-phenylenediamine (5.4 g, 50 mmol) and ethyl 4,4,4-trifluoroacetoacetate (11 g, 60 mmol) in ethanol (100 mL) was heated at reflux overnight to give rise to a yellow slurry. P-Toluenesulfonic acid monohydrate (0.19 g, 1.0 mmol) was added and the reaction mixture was allowed to stir at reflux for additional 24 h. The reaction was cooled to room temperature to generate a large amount of solid. Filtration from the solid (Compound **512** as major product) and removal solvent provided the crude mixture. Chromatography of the mixture on a silica gel column afforded Compound **554** (1.4 g, 11%) as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 7.70 (dq, J = 9.5, 2.1, 1 H), 7.05-7.01 (m, 2 H), 6.86 (s, 1 H), 5.44 (bs, 2 H), 4.47 (q, J = 7.0, 2 H), 1.39 (t, J = 7.0, 3 H).

7-(1-Phenylaminocarbonylisopropyl)amino-2-ethoxy-4-trifluoromethylquinoline (Compound **555**, Structure **68** of Scheme XIII):

To a flask charged with NaH (40 mg, 60% in mineral oil, 1.0 mmol) in THF (2 mL) was added a solution of Compound **554** (128 mg, 0.5 mmol) in THF (2 mL). A solution of N-phenyl-2-bromobutyratamide (121 mg, 0.5 mmol) in THF (2 mL) was introduced slowly in 15 min. and

the reaction mixture was stirred at room temperature for 1h, then quenched with water and extracted with EtOAc. Removal of solvent and chromatography of the crude residue afforded Compound **555** as a white solid: [1]H NMR (400 MHz, $CDCl_3$) 8.74 (s, 1 H), 7.81 (dq, *J* = 9.5, 2.1, 1 H), 7.50 (d, *J* = 7.5, 2 H), 7.31 (t, *J* = 7.5, 2 H), 7.11 (t, *J* = 7.5, 1 H), 7.00 (d, *J* = 2.5, 1 H), 6.96 (s, 1 H), 6.85 (dd, *J* = 9.5, 2.5, 1 H), 4.47 (q, *J* = 7.2, 2 H), 1.67 (s, 6 H), 1.39 (t, *J* = 7.2, 3 H).

7-(1-Phenylaminocarbonylisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **553**, Structure **69** of Scheme XIII):

Treatment of Compound **555** with hydriodic acid (57% aqueous) at 60 °C for 2 h and standard work-up provided Compound **553** as a yellow solid: [1]H NMR (400 MHz, $CDCl_3$) 11.10 (bs, 1 H), 7.61 (dq, *J* = 9.5, 2.1, 1 H), 7.48 (d, *J* = 7.5, 2 H), 7.27 (t, *J* = 7.5, 2 H), 7.11 (t, *J* = 7.5, 1 H), 6.78 (s, 1 H), 6.61 (dd, *J* = 9.5, 2.5, 1 H), 6.54 (d, *J* = 2.5, 1 H), 1.64 (s, 6 H).

EXAMPLE 284

7-(2-Hydroxy-1,1-dimethylethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 556, Structure 72 of Scheme XIII)

7-(N-methyl-N-1-Phenylaminocarbonylisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **557**, Structure **70** of Scheme XIII):

To a flask charged with NaH (80 mg, 60% in mineral oil, 2.0 mmol) in THF (3 mL) was added a solution of Compound **554** (Structure **67** of Scheme XIII) (256 mg, 1.0 mmol) in THF (3 mL). A solution of N-phenyl-2-bromobutyratamide (242 mg, 1.0 mmol) in THF (4 mL) was introduced slowly in 15 min. and the reaction mixture was stirred at room temperature for 1h. The reaction mixture was treated with iodomethane (0.3 mL, 4.5 mmol) and stirred for additional 1h, then quenched with water and extracted with EtOAc. The crude mixture was treated with hydriodic acid at 40 °C for 3 h and quenched with 10% NaOH. Extraction with EtOAc and removal of solvent provided the crude product. Purification by chromatography afforded Compound **557** as a white solid (220 mg, 50%).

7-(N-2-Formyl-2-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **558**, Structure **71** of Scheme XIII) and 7-(2-Hydroxy-1,1-dimethylethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **556**, Structure **72** of Scheme XIII):

Compound **557** (200 mg, 0.45 mmol) in THF (5 mL) was treated with DIBAL-H (1.5 mL, 1.0 M in toluene) at –60 °C for 1h. Standard work-up followed by chromatography afforded Compound **558** (50 mg, 36%) and Compound **556** (70 mg, 51%). Compound **556** was isolated as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 7.42 (dq, J = 8.8, 1.9, 1 H), 6.85 (d, J = 2.1, 1 H), 6.72 (dd, J = 8.8, 2.1, 1 H), 6.48 (s, 1 H), 5.54 (s, 1 H), 3.60 (s, 2 H), 1.86 (s, 6 H).

EXAMPLE 285

7-(1,1-Dimethylallyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 559, Structure 73 of Scheme XIII)

To a mixture of Ph_3PCH_2Br-HCl (72 mg, 0.20 mmol) and $NaN(SiMe_3)_2$ (0.20 mL, 1.0 M in THF) in THF (3 mL) at room temperature was added a THF solution of Compound **558** (Structure **71** of Scheme XIII) (15 mg, 0.050 mmol) and the resulting mixture was stirred for 1h. Standard work-up followed by chromatography afforded Compound **559** (10 mg, 83%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) 11.71 (bs, 1 H), 7.52 (dq, J = 8.8, 1.5, 1 H), 6.70 (s, 1 H), 6.63 (dd, J = 9.1, 2.2, 1 H), 6.60 (d, J = 2.2, 1 H), 5.96 (dd, J = 17.4, 10.6, 1 H), 5.27 (d, J = 17.4, 1 H), 5.21 (d, J = 10.6, 1 H), 4.44 (s, 1 H), 1.46 (s, 6 H).

EXAMPLE 286

7-(1,1-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound 560, Structure 74 of Scheme XIII)

A solution of Compound **285** (Structure **73** of Scheme XIII) (5.0 mg, 0.017 mmol) in EtOAc was hydrogenated in the presence of a catalytic amount 10% Pd/C to afforded Compound **560** (3.0 mg, 60%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) 11.71 (bs, 1 H), 7.53 (dq, J = 8.8, 1.5, 1 H), 6.70 (s, 1 H), 6.61 (dd, J = 9.1, 2.2, 1 H), 6.57 (d, J = 2.2, 1 H), 4.20 (bs, 1 H), 1.78 (q, J = 7.4, 2 H), 1.39 (s, 6 H), 0.90 (t, J = 7.4, 3 H).

EXAMPLE 287

7-(1-Methyl-1-acetylenylpropyl)amino]-4-(trifluoromethyl)-2(1*H*)-quinolinone

(Compound 561, Structure 75 of Scheme XIV)

To a mixture of Compound **512** (Structure **61a** of Scheme XIV) (1.8 g, 8.0 mmol), CuCl (40 mg, 0.40 mmol) in 50 mL THF was added triethylamine (0.89 g, 8.8 mmol) and 3-acetoxy-3-

methyl-1-pentyne (1.1 g, 8.0 mmol). After 4h, the mixture was partitioned between EtOAc (60 mL) and sat'd NH_4Cl (60 mL), and the aqueous layer was extracted with EtOAc (60 mL). The organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (1:1:1 EtOAc:hexanes: CH_2Cl_2) afforded 0.31 g (13%) of Compound **561** as a yellow solid: R_f 0.30 (1:1:1 EtOAc:hexanes: CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) 12.1 (bs, 1H), 7.55-7.65 (m, 1 H), 6.93 (dd, J = 9.0, 2.3, 1 H), 6.88 (d, J = 2.2, 1 H), 6.75 (s, 1 H), 4.36 (s, 1 H), 2.49 (s, 1 H), 1.80-2.00 (m, 2 H), 1.60 (s, 3 H), 1.08 (t, J = 7.4, 3 H).

EXAMPLE 288

7-(1-Ethyl-1-methylpropyl)amino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound 562, Structure 76 of Scheme XIV)

A solution of Compound **561** (Structure 75 of Scheme XIV) (16 mg, 0.052 mmol) in EtOAc/EtOH (2:1) was hydrogenated in the presence of 10% Pd-C (2.4 mg, 15 wt %) to afford 10 mg (63%) of Compound **562** as a yellow foam: R_f 0.30 (1:1:1 EtOAc:hexanes: CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) 12.3 (bs, 1 H), 7.48-7.56 (m, 1 H), 6.70 (s, 1 H), 6.58-6.65 (m, 2 H), 4.14 (broad s, 1 H), 1.76-1.90 (m, 2 H), 1.62-1.74 (m, 2 H), 1.29 (s, 3 H), 0.87 (t, J = 7.4, 3 H).

EXAMPLE 289

8-Methyl-7-(3-methyl-2-butenyl)amino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound 563, Structure 79 of Scheme XV, where R = 3-methyl-2-butenyl)

2-(*tert*-Butyloxycarbamoyl)-6-(3-methyl-2-butenyl)aminotoluene (Compound **564**, Structure 77 of Scheme XV, R = 3-methyl-2-butenyl):

To an oven-dried 25-mL r.b. flask containing 2-amino-6-(*tert*-butyloxycarbamoyl)toluene (0.50 g, 2.3 mmol) in 10 mL glacial acetic acid at room temperature was added 3-methyl-2-butenal (senecialdehyde, 0.43 mL, 4.5 mmol, 2.0 equiv) and sodium cyanoborohydride (0.70 g, 11 mmol, 5.0 equiv), and the mixture was allowed to stir for 6 h. The mixture was then neutralized to pH 8 with the careful addition of saturated $NaHCO_3$. The mixture was then extracted with EtOAc (2 x 40 mL), and the combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash chromatography (hexanes:EtOAc, 10:1 to 4:1 gradient) afforded 611 mg (94%) of Compound **564** as a white

solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.09 (t, 1H, J = 8.0, 4-H), 6.96 (br d, 1H, J = 8.0, 3-H), 6.46 (d, 1H, J = 8.1, 5-H), 6.18 (br s, 1H, CON*H*), 5.36 (t, 1H, J = 6.7, C=C*H*), 3.70 (d, 2H, J = 6.7, NHCH_2CH=C), 3.40 (br s, 1H, ArN*H*CH_2), 2.00 (s, 3H, 1-CH_3), 1.76 and 1.71 [2s, 2 x 3H, CH=C(CH_3)$_2$], 1.50 [s, 9H, (CH_3)$_3$CO].

2-Amino-6-(3-methyl-2-butenyl)aminotoluene (Compound **565**, Structure **78** of Scheme XV, R = 3-methyl-2-butenyl):

Treatment of Compound **564** with TFA removed the *tert*-butoxy protection group to give Compound **565** in high yield.

8-Methyl-7-(3-methyl-2-butenyl)amino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **563**, Structure **79** of Scheme XV, where R = 3-methyl-2-butenyl):

This compound was prepared in a similar fashion as that described in Example 243, but using Compound **565** (611 mg, 2.10 mmol) in place of 1,3-phenylenediamine. Compound **563** (261 mg, 40%) was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 9.12 (br s, 1H, CON*H*), 7.61 (br d, 1H, J = 7.6, 5-H), 6.71 (s, 1H, 7-H), 6.68 (d, 1H, J = 9.1, 6-H), 5.34 (t, 1H, J = 5.9, C=C*H*), 4.03 (br s, 1H, ArN*H*CH_2), 3.84 (t, 2H, J = 5.8, NHCH_2CH=C), 2.13 (s, 3H, 8-CH_3), 1.79 and 1.75 [2s, 2 x 3H, CH=C(CH_3)$_2$].

EXAMPLE 290

8-Methyl-7-(3-methylbutyl)amino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound 566, Structure 79 of Scheme XV, where R = 3-methylbutyl)

To an oven-dried 25-mL r.b. flask containing Compound **289** (Structure **79** of Scheme XV, where R = 3-methyl-2-butenyl) (74 mg, 0.24 mmol) in 2 mL 1,2-dichloroethane was added 0.3 mL TFA and 0.5 mL triethylsilane, and the mixture was heated to reflux for 8 h. Upon cooling to rt, the mixture was added to 5 mL saturated $NaHCO_3$ and extracted with 10 mL EtOAc. The organic layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, hexanes/EtOAc, 4:1 to 0:1 gradient), affording 28 mg (37%) of Compound **566** as a fluorescent yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 9.09 (br s, 1H, CON*H*), 7.61 (br d, 1H, J = 7.6, 5-H), 6.70 (s, 1H, 7-H), 6.69 (d, 1H, J = 9.1, 6-H), 3.99 (br s, 1H, (ArN*H*CH_2), 3.11 [t, 2H, J = 6.8,

$NHCH_2CH_2CH(CH_3)_2$], 2.11 (s, 3H, 8-CH_3), 1.7-1.4 [m, 3H, $NHCH_2CH_2CH(CH_3)_2$], 0.98 [d, 2 x 3H, J = 6.7, $CH(CH_3)_2$].

EXAMPLE 291

8-Methyl-7-propylamino-4-(trifluoromethyl)-2(1*H*)-quinolinone

(Compound 567, Structure 79 of Scheme XV, where R = propyl)

3-amino-2-methyl-N-propylaminobenzene (Compound **568**, Structure **78** of Scheme XV, where R = propyl):

To a solution of 2-methyl-3-nitroaniline (0.5 g, 3.3 mmol) and MeOH (20 mL) was added propionaldehyde (2.3 mL, 33 mmol), AcOH (1.9 mL, 33 mmol), and $NaBH_3CN$ (2 g, 33 mmol). Reaction was stirred at rt for 2 hours then quenched with H_2O and concentrated *in vacuo*. Diluted with EtOAc (20 mL) and adjusted to pH = 7 with saturated $NaHCO_3$. Washed organic layer with H_2O (3x 10 mL) and brine (3x 10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by flash chromatography (5% EtOAc/hex) to afford 0.7 g of the 2-methyl-3-nitro-N-propylaminobenzene. A solution of the product and EtOAc (25 mL) was hydrogenated over 10% Pd/C (70 mg) at rt and 1 atm. After 15 hours filtered reaction mixture through a pad of Celite and concentrated the filtrate to afford the desired Compound **568** (0.10 g) as yellow oil.

Compound **568** was dissolved in EtOH (7 mL) and treated with ethyl-4,4,4-trifluoromethylacetoacetate (0.11 mL). This reaction mixture was heated to reflux for 15 hrs. Concentrated in vacuo and purified by flash chromatography (50% EtOAc/hex) to afford the tertiary alcohol (100 mg). The tertiary alcohol was dissolved in toluene and treated with p-TsOH (50 mg) and the reaction was heated to reflux for 15 hrs. The reaction mixture was concentrated in vacuo to afford a light red solid which was then washed with EtOH to afford 48 mg (5% overall yield) of Compound **567** as a white solid: ^1H NMR (400 MHz, CD_3OD) 7.56 (m, 1 H), 6.78 (d, J = 9.2, 1 H), 6.56 (s, 1 H), 3.27 (m under solvent peak, 2 H), 2.20 (3 H), 1.68 (m, 2 H), 1.01 (t, J = 7.4, 3 H).

EXAMPLE 292

8-Methyl-7-isobutylamino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound 569, Structure 79 of Scheme XV, where R = isobutyl)

3-Amino-2-methyl-N-isobutylaminobenzene (Compound **570**, Structure **78** of Scheme XV, where R = isobutyl):

To a solution of 2-methyl-3-nitroaniline (Structure **28b** of Scheme XV) (0.5 g, 3.3 mmol) and MeOH (20 mL) was added isobutyraldehyde (3 mL, 33 mmol), AcOH (1.9 mL, 33 mmol), and $NaBH_3CN$ (2 g, 33 mmol). Reaction was stirred at rt for 2 hours then quenched with H_2O and concentrated *in vacuo*. Diluted with EtOAc (20 mL) and adjusted to pH = 7 with saturated $NaHCO_3$. Washed organic layer with H_2O (3x 10 mL) and brine (3 x 10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by flash chromatography (5% EtOAc/hex) to afford 0.9 g of the N-isobutylamino-2-methyl-3-nitrobenzene. A solution of the product and EtOAc (25 mL) was hydrogenated over 10% Pd/C (90 mg) at room temperature and 1 atm. After 15 hours filtered reaction mixture through a pad of Celite and concentrated the filtrate to afford Compound **570** (0.45 g) as a white solid.

Compound **570** (100 mg) was dissolved in EtOH (7 mL) and treated with ethyl-4,4,4-trifluoromethylacetoacetate (0.1 mL). This reaction mixture was heated to reflux for 15 hrs. Concentrated in vacuo and purified by flash chromatography (50% EtOAc/hex) to afford the tertiary alcohol intermediate. The tertiary alcohol was dissolved in toluene (7 mL) and treated with p-TsOH (10 mg) and the reaction was heated to reflux for 15 hrs. The reaction mixture was concentrated in vacuo then purified by flash chromatography (10% EtOAc/hexane to 100% EtOAc gradient) to afford 112 mg (67%) of Compound **569** as a white solid: ^1H NMR (400 MHz, CD_3OD) 7.65 (d, J = 9.2, 1 H), 6.96 (d, J = 9.2, 1 H), 6.73 (s, 1 H), 3.17 (d, J = 7.1, 2 H), 2.20 (s, 3 H), 1.02 (d, J = 6.7, 6 H).

EXAMPLE 293

7-Amino-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 571, Structure 83 of Scheme XVI)

2,4-Dinitrophenyl-(2,2,2-trifluoroethyl)ether (Compound **572**, Structure **81** of Scheme XVI):

In a 100 mL flask, a solution of 2,4-dinitrofluorobenzene (1.0 mL) in acetone (20 mL) was treated with 2,2,2-trifluoroethanol (1.2 mL) and Et_3N (1.2 mL). The reaction mixture was warmed to 45-50 °C for 3 h, the volatiles were removed in vacuo, and the residue was dissolved in EtOAc (40 mL). The organic layer was washed with water (50 mL) and brine (50 mL). The aqueous layers were extracted with EtOAc (2 x 30 mL). The organic layers were combined, dried (K_2CO_3), filtered through a pad of Celite, and concentrated to afford orange oil. Purification by silica gel chromatography (hexane:EtOAc, 4:1) to afford 2.1 g (99%) of Compound **572** as an orange oil: ^{1}H NMR (400 MHz, $CDCl_3$) 8.80 (d, J = 2.8, 1 H), 8.49 (dd, J = 8.3, 2.8, 1 H), 7.25 (d, J = 8.3, 1 H), 4.63 (q, J = 7.6, 2 H).

2,4-Diaminophenyl(2,2,2-trifluoroethyl)ether (Compound **573**, Structure **82** of Scheme XVI):

In a 100 mL flask, a solution of Compound **572** (0.85 g) in 1:1 EtOH:EtOAc (40 mL) was treated with 10% Pd/C (0.2 g) and stirred under an atmosphere of hydrogen for 2 h. The reaction mixture was filtered and concentrated to afford 0.62 g (92%) of Compound **573** as a white solid: ^{1}H NMR (400 MHz, acetone-d_6) 6.67 (d, J = 8.5, 1 H), 6.12 (d, J = 2.6, 1 H), 5.92 (dd, J = 8.5, 2.6, 1 H), 4.39 (q, J = 8.9, 2 H), 4.28 (br exch s, 2 H), 4.17 (br exch s, 2 H).

7-Amino-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **571**, Structure **83** of Scheme XVI):

Compound **573** (0.62 g) was dissolved in toluene (20 mL), treated with 4,4,4-trifluoroacetoacetate (0.58 mL), and the reaction mixture was heated to reflux for 1 h. To this solution was added $ZnCl_2$ (0.26 g) and the reaction mixture was heated to reflux for 2 h. *p*-Toluenesulfonic acid hydrate (0.1 g) was added and the reaction mixture maintained a reflux for 1h. The bulk of the volatiles were removed in vacuo and the residue was poured into 0.5 N $NaHSO_4$ (20 mL). The reaction mixture was extracted with EtOAc (3 x 30 mL). The extracts were washed with water (20 mL) and brine (20 mL), combined, dried ($MgSO_4$), filtered, and concentrated. The crude material was suspended in 15:1 CH_2Cl_2:MeOH and the yellow solid collected by filtration to afford 471 mg (43%) of Compound **571** as a yellow-white solid: R_f 0.14 (15:1 CH_2Cl_2:MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) 11.94 (br s, 1 H), 7.01 (s, 1 H), 6.66 (s, 1 H), 6.51 (s, 1 H), 6.01 (br exch s, 2 H), 4.76 (q, J = 8.8, 2 H).

EXAMPLE 294

7-Isobutylmino-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **574**, Structure **84** of Scheme XVI, where R = isobutyl)

In a 20 mL r.b. flask, a solution of Compound **571** (Structure **83** of Scheme XVI) (39 mg) in AcOH (1 mL) was treated with isobutyraldehdye (16 μL) and $Na(CN)BH_3$ (11 mg). The reaction mixture was stirred overnight, poured into 20% KOH (6 mL), and extracted with EtOAc (3 x 6 mL). The extracts were washed with 20% KOH (6 mL) and brine (6 mL); combined, dried ($MgSO_4$), filtered, and concentrated. Purification by silica gel chromatography (CH_2Cl_2:MeOH, 30:1 to 15:1 gradient) afforded 19 mg (54%) of Compound **574** as a yellow solid: R_f 0.32 (15:1 CH_2Cl_2:MeOH); ^1H NMR (400 MHz, acetone-d_6) 10.72 (br exch s, 1 H), 7.15 (s, 1 H), 6.69 (s, 1H), 6.54 (s, 1 H), 5.77 (br exch s, 1 H), 4.77 (q, J = 8.5, 2 H), 3.11 (t, J = 6.4, 2 H), 0.99 (d, J = 6.7, 6 H). The methine proton is obscured by the acetone heptet.

EXAMPLE 295

7-(2-Picolylamino)-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone

(Compound **575**, Structure **84** of Scheme XVI, R = 2-picolyl)

In a 20 mL flask, a solution of Compound **293** (Structure **83** of Scheme XVI) (38 mg) in AcOH (1 mL) was treated with 2-pyridinecarboxaldehyde (16 μL) and $Na(CN)BH_3$ (11 mg). The reaction mixture was stirred overnight, poured into 20% KOH (6 mL), and extracted with EtOAc (3 x 6 mL). The extracts were washed with 20% KOH (6 mL) and brine (6 mL); combined, dried (MgSO4), filtered, and concentrated. Purification by silica gel chromatography (CH_2Cl_2:EtOAc:MeOH,85:10:5) afforded 31 mg (60%) of Compound **295** as a yellow solid: R_f 0.18 (CH_2Cl_2:EtOAc:MeOH,85:10:5); ^1H NMR (400 MHz, acetone-d_6) 10.80 (br exch s, 1H), 8.56 (d, J = 8.4, 1H), 7.77 (m, 1H), 7.41 (d, J = 7.6, 1H), 7.25 (m, 1H), 7.20 (s, 1H), 6.72 (br exch s, 1 H), 6.60 (s, 1 H), 6.55 (s, 1 H), 5.77 (br exch s, 1 H), 4.85 (q, J = 8.5, 2 H), 4.61 (d, J = 5.6, 2 H).

EXAMPLE 296

7-Amino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 576, Structure 88 of Scheme XVII, R^1 = methyl, $R^2 = R^3$ = H)

This compound was prepared by the following General Procedure XVII (Condensation of 4-alkyl-1,3-phenylenediamine with acetoacetates or their corresponding hydrates followed by Knorr reaction mediated by *p*-toluenesulfonic acid):

To a solution of 4-alkyl-1,3-phenylenediamine (Structure **87** of Scheme XVII) in benzene or toluene (10 mL/mmol) under N_2 was added an acetoacetate derivative (1.2 equiv) and the reaction mixture was heated at reflux for 4-8 h, then cooled and concentrated under reduced pressure. The crude mixture was then triturated with Et_2O:Hexane (3:1, 4 mL/mmol), then redissolved in toluene:EtOH (10:1, 10 mL/mmol) and treated with *p*-toluenesulfonic acid. The reaction mixture was then heated at reflux for 1-2 h. After cooling, the excess solvent was removed and the crude product redissolved in EtOAc (100 mL/mmol). The organic solution was washed with saturated $NaHCO_3$ (2 x 25 mL/mmol), Brine (25 mL/mmol), dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford the desired quinolinone as a white solid. If needed, the desired product was further purified by silica gel chromatography as indicated.

Compound **576** was prepared from 2,4-diaminotoluene (1.0 g, 8.2 mmol) in 40% yield (0.80 g) as yellow needles: ^{1}H NMR (400 MHz, DMSO-d_6) 11.00 (br s, 1 H), 7.21 (s, 1 H), 6.54 (s, 1 H), 6.45 (s, 1 H), 2.10 (s, 3 H).

EXAMPLE 297

7-Amino-6-ethyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 577, Structure 88 of Scheme XVII, where R^1 = ethyl, $R^2 = R^3$ = H)

2-Ethyl-5-nitroaniline (Compound **578**, Structure **86** of Scheme XVII, where R^1 = ethyl, $R^2 = R^3$ = H):

This compound is prepared according to the following General Procedure XVIII (nitration of amine):

A solution of an alkylaniline in conc H_2SO_4 (6 mL/mmol) was cooled to –10 ° C, then treated with a 25% solution of fuming HNO_3 (1.0 equiv) dissolved in H_2SO_4. The rate of addition is adjusted so as to keep the temperature below –5 ° C. After complete addition of the

HNO_3 solution, the reaction was allowed to stir at −10 ° C for 15 min, warmed to room temperature, poured over NaOH pellets (0.7 g/mL H_2SO_4) and ice. The aqueous solution was stirred over ice to dissolve all the NaOH, filtered then washed with water (2.0 mL/mmol) to afford the desired product as an yellow-orange solid.

Compound **578** was prepared from 2-ethylaniline (200 mg, 1.62 mmol) in 97% yield as a yellow oil: ^1H NMR (400 MHz, $CDCl_3$) 7.59 (dd, J = 8.3, 2.3, 1 H), 7.50 (d, J = 2.2, 1 H), 7.17 (d, J = 8.3, 1 H), 3.90 (bs, 2 H), 2.56 (q, J = 7.6, 2 H), 1.28 (t, J = 7.4, 3 H).

4-Ethyl-1,3-phenylenediamine (Compound **579**, Structure **87** of Scheme XVII, where R^1 = ethyl, $R^2 = R^3$ = H):

This compound is prepared according to General Procedure III from Compound **578** (110 mg, 0.66 mmol) in 76% yield. Compound **579** was isolated as a light brown oil: ^1H NMR (400 MHz, $CDCl_3$) 6.84 (d, J = 8.0, 1 H), 6.12 (dd, J = 8.0, 2.3, 1 H), 6.06 (d, J = 2.3, 1 H), 3.50 (bs, 4 H), 2.42 (q, J = 7.5, 2 H), 1.19 (t, J = 7.5, 3 H).

7-Amino-6-ethyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **577**, Structure **88** of Scheme XVII, where R^1 = ethyl, $R^2 = R^3$ = H):

This compound was prepared according to General Procedure XVII in Example 296 from Compound **579** (69 mg, 0.50 mmol) and ethyl-4,4,4-trifluoroacetoacetate (0.09 mL, 0.62 mmol) and purified by flash chromatography ($MeOH/CH_2Cl_2$, 1% to 4% gradient), to afford 63 mg (52%) of Compound **577** as a yellow solid: ^1H NMR (400 MHz, DMSO-d_6) 11.80 (s, 1 H), 7.20 (s, 1 H), 6.54 (s, 1 H), 6.42 (s, 1 H), 5.98 (s, 2 H), 2.50 (m, 2 H), 1.14 (t, J = 7.4, 3 H).

EXAMPLE 298

7-Amino-6-propyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **580**, Structure **88** of Scheme XVII, where R^1 = proyl, $R^2 = R^3$ = H)

This compound is prepared in a similar fashion as that described in Examples 297 and 1, General Procedure XVIII, and III but using 2-propylaniline (Structure **85** of Scheme XVII, where R^1 = propyl, $R^2 = R^3$ = H) (0.20 mL, 1.42 mmol) in place of 2-ethylaniline.

Data for 2-propyl-5-nitroaniline (Structure **86** of Scheme XVII, where R^1 = propyl, R^2 = R^3 = H): ^1H NMR (400 MHz, $CDCl_3$) 7.56 (dd, J = 8.2, 2.3, 1 H), 7.50 (d, J = 2.3, 1 H), 7.14 (d, J = 8.3, 1 H), 3.90 (bs, 2 H), 2.52 (t, J = 7.8, 2 H), 1.66 (sex, J = 7.5, 2 H), 1.01 (t, J = 7.3, 3 H).

Data for 4-propyl-1,3-phenylenediamine (Structure **87** of Scheme XVII, where R^1 = propyl, $R^2 = R^3$ = H): ^1H NMR (400 MHz, $CDCl_3$) 6.81 (d, J = 8.1, 1 H), 6.09 (dd, J = 8.2, 2.3, 1 H), 6.02 (d, J = 2.3, 1 H), 3.50 (bs, 4 H), 2.40 (t, J = 7.8, 2 H), 1.58 (sex, J = 7.5, 2 H), 0.97 (t, J = 7.3, 3 H).

Data for Compound **580** (Structure **88** of Scheme XVII, where R^1 = propyl, $R^2 = R^3$ = H): ^1H NMR (400 MHz, DMSO-d_6) 11.78 (s, 1 H), 7.17 (s, 1H), 6.52 (s, 1 H), 6.41 (s, 1 H), 5.96 (s, 2 H), 2.45 (t, J = 7.6, 2 H), 1.52 (m, 2 H), 0.92 (t, J = 7.3, 3 H).

EXAMPLE 299

7-Amino-6-*sec*-butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **581**, Structure **88** of Scheme XVII, where R^1 = *sec*-butyl, $R^2 = R^3$ = H)

This compound is prepared in a similar fashion as that described in Examples 297 and 1, General Procedure XVIII and III but using 2-*s*-butyl-aniline (Structure **85** of Scheme XVI, where R^1 = *sec*-butyl, $R^2 = R^3$ = H) (0.20 mL, 1.28 mmol) in place of 2-ethylaniline.

Data for 2-*sec*-butyl-5-nitroaniline (Structure **86** of Scheme XVII, where R^1 = *sec*-butyl, $R^2 = R^3$ = H): ^1H NMR (400 MHz, $CDCl_3$) 7.60 (dd, J = 8.5, 2.3, 1 H), 7.50 (d, J = 2.4, 1 H), 7.19 (d, J = 8.5, 1H), 3.92 (bs, 2 H), 2.67 (sex, J = 6.9, 1 H), 1.66 (m, 2 H), 1.25 (d, J = 6.8, 3 H), 0.91 (t, J = 7.3, 3 H).

Data for 4-*sec*-butyl-1,3-phenylenediamine (Structure **87** of Scheme XVII, where R^1 = *sec*-butyl, $R^2 = R^3$ = H): ^1H NMR (400 MHz, $CDCl_3$) 6.86 (d, J = 8.3, 1 H), 6.14 (dd, J = 8.2, 2.4, 1 H), 6.08 (d, J = 2.3, 1 H), 3.60 (bs, 4 H), 2.53 (sex, J = 6.9, 1H), 1.52 (m, 2 H), 1.15 (d, J = 6.7, 3 H), 0.86 (t, J = 7.2, 3 H).

Data for Compound **581** (Structure **88** of Scheme XVII, where R^1 = *sec*-butyl, $R^2 = R^3$ = H): ^1H NMR (400 MHz, DMSO-d_6) 11.78 (s, 1 H), 7.19 (s, 1 H), 6.53 (s, 1 H), 6.42 (s, 1 H), 5.99 (s, 2 H), 2.80 (m, 1 H), 1.56-1.48 (m, 2 H), 1.10 (t, J = 3.8, 3 H), 0.83 (t, J = 7.3, 3 H).

EXAMPLE 300

7-Amino-6-cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **582**, Structure **88** of Scheme XVII, where R^1 = cyclohexyl, $R^2 = R^3$ = H)

4-Cyclohexyl-3-nitroaniline (Compound **583**, Structure **91** of Scheme XVII):

This compound is prepared according to General Procedure XVIII in Example 297 from 4-cyclohexyl-aniline (285 mg, 1.62 mmol) and HNO_3 (90 mg, 1.62 mmol) in 94% yield. Compound **583** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.20 (d, J = 8.4, 1 H), 6.97 (d, J = 2.5, 1 H), 6.81 (dd, J = 8.5, 2.5, 1 H), 3.78 (bs, 2 H), 2.85 (m, 1 H), 1.83 (m, 4 H), 1.75 (m, 1 H), 1.36 (m, 4 H), 1.23 (m, 1 H).

4-Cyclohexyl-1,3-phenylenediamine (Compound **584**, Structure **87** of Scheme XVII, where R^1 = cyclohexyl, R^2 = R^3 = H):

This compound is prepared according to General Procedure III in Example 1 from Compound **583** (353 mg, 1.60 mmol) and purified by flash chromatography ($MeOH/CH_2Cl_2$, 0% to 2% gradient). Compound **582** was isolated in 96% yield as a light brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) 6.88 (d, J = 8.1, 1 H), 6.15 (dd, J = 8.1, 2.3, 1 H), 6.06 (d, J = 2.4, 1 H), 3.48 (bs, 4 H), 2.35 (m, 1 H), 1.84 (m, 4 H), 1.75 (m, 1 H), 1.37 (m, 4 H), 1.25 (m, 1 H).

7-Amino-6-cyclohexyl-1,2-dihydro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **582**, Structure **88** of Scheme XVII, where R^1 = cyclohexyl, R^2 = R^3 = H):

This compound was prepared according to General Procedure XVII in Example 296 from Compound **584** (69 mg, 0.50 mmol) and ethyl 4,4,4-trifluoroacetoacetate (0.09 mL, 0.62 mmol) and purified by flash chromatography ($MeOH/CH_2Cl_2$, 1% to 4% gradient). Compound **582** was isolated in 52% yield as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 11.78 (s, 1 H), 7.21 (s, 1 H), 6.53 (s, 1 H), 6.41 (s, 1 H), 5.99 (s, 2 H), 2.60 (t, J = 11.6, 1 H), 1.82-1.69 (m, 5 H), 1.50-1.41 (m, 2 H), 1.29-1.21 (m, 3 H).

EXAMPLE 301

6-Ethyl-7-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 585, Structure 89 of Scheme XVII, where R^1 = ethyl, R^2 = H, R^3 = 2,2,2-trifluoroethyl)

This compound is prepared in a similar fashion as that described in Example 9, General Procedure VI but using Compound **577** (Structure **88** of Scheme XVII, where R^1 = ethyl, R^2 = R^3 = H) and TFA in place of Compound **200** and 2,2-difluoroacetic acid. Compound **585** was isolated as a white solid: ^{1}H NMR (400 MHz, CD_3CN) 9.72 (bs, 1 H), 7.42 (s, 1 H), 6.63 (s, 1 H), 6.60 (s, 1 H), 5.30 (bs, 1 H), 3.96 (m, 2H), 2.58 (q, J = 7.5, 2 H), 1.20 (t, J = 7.7, 3 H).

EXAMPLE 302

6-Ethyl-7-methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 586, Structure 89 of Scheme XVII, where R^1 = ethyl, R^2 = H, R^3 = methyl)

This compound is prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **577** (Structure **88** of Scheme XVII, where R^1 = ethyl, R^2 = R^3 = H) and paraformaldehyde in place of Compound **200** and propionaldehyde. Compound **586** was isolated as a white solid: ^{1}H NMR (400 MHz, CD_3CN) 10.85 (bs, 1 H), 7.54 (s, 1 H), 7.13 (s, 1 H), 6.73 (s, 1 H), 2.76 (q, *J* = 7.5, 2 H), 1.26 (t, *J* = 7.4, 3 H).

EXAMPLE 303

6-Ethyl-7-dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 587, Structure 89 of Scheme XVII, where R^1 = ethyl, R^2 = R^3 = methyl)

This compound is prepared in a similar fashion as that described in Example 15, General Procedure VIII but using Compound **577** (Structure **88** of Scheme XVII, where R^1 = ethyl, R^2 = R^3 = H) a in place of Compound **200**. Compound **587** was isolated as a white solid: ^{1}H NMR (400 MHz, CD_3CN) 11.66 (bs, 1 H), 7.60 (s, 1 H), 6.90 (s, 1 H), 6.88 (s, 1 H), 2.83 (s, 6 H), 2.76 (q, *J* = 7.5, 2H), 1.29 (t, *J* = 7.5, 3 H).

EXAMPLE 304

6-Isobutyl-7-methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 588, Structure 89 of Scheme XVII, where R^1 = isobutyl, R^2 = H, R^3 = methyl)

This compound is prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **581** (Structure **88** of Scheme XVII; where R^1 = isobutyl, R^2 = R^3 = H) and paraformaldehyde in place of Compound **200** and propionaldehyde. Compound **588** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.36 (bs, 1 H), 7.43 (d, *J* = 1.8, 1 H), 6.74 (s, 1 H), 6.40 (s, 1 H), 4.39 (bm, 1 H), 3.00 (d, *J* = 5.0, 3 H), 2.58 (dt, *J* = 6.8, 1 H), 1.76-1.68 (m, 1 H), 1.64-1.57 (m, 1 H), 1.25 (d, *J* = 2.8, 3 H), 0.92 (t, *J* = 7.6, 3 H).

EXAMPLE 305

7-(1-Morpholino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 589, Structure 88 of Scheme XVII, where R^1 = H, NR^2R^3 = morpholino)

1-(3-Nitrophenyl)morpholine (Compound **590**, Structure **86** of Scheme XVII, where R^1 = H, NR^2R^3 = morpholino):

In a 100 mL flask, a solution of 1-phenylmorpholine (Structure **85** of Scheme XVII, where R^1 = H, NR^2R^3 = morpholino) (0.63 g) in concentrated sulfuric acid (5 mL) was cooled to –5 °C. To this solution, 90% fuming nitric acid (0.17 mL) was added dropwise via syringe over a 3-minute period. The reaction mixture was stirred for 5 min, poured onto ice (50 g), and neutralized by portionwise addition of K_2CO_3 (~ 5 g). The reaction mixture was poured into water (20 mL) and extracted with CH_2Cl_2 (3x 50 mL). The extracts were washed with saturated $NaHCO_3$ (50 mL), combined, dried ($MgSO_4$), filtered through a pad of Celite, and concentrated to afford 0.78 g of an orange solid which was purified by silica gel chromatography (hexane:EtOAc, 8:1) to afford 0.33 g (41%) of Compound **590** as orange crystals: ^{1}H NMR (400 MHz, $CDCl_3$) 7.71 (m, 2 H), 7.40 (t, *J* = 8.1, 1 H), 7.18 (dd, *J* = 8.5, 2.4, 1 H), 3.89 (t, *J* = 4.8, 4 H), 3.25 (t, *J* = 4.8, 4 H).

7-(1-Morpholino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **589**, Structure **88** of Scheme XVII, where R^1 = H, NR^2R^3 = morpholino):

In a 100 mL flask, a solution of Compound **590** (0.33 g) in EtOAc (12 mL) was treated with 10% Pd/C (50 mg) and stirred under an atmosphere of H_2 for 14 h. The reaction mixture was filtered and concentrated to afford 1-(3-aminophenyl)morpholine (Compound **591**, Structure **87** of Scheme XVII, where R^1 = H, NR^2R^3 = morpholino) as a white solid, which was used without further purification. Compound **591** was dissolved in EtOH (10 mL), treated with ethyl 4,4,4-trifluoroacetoacetate (0.27 mL), and stirred at room temperature for 10 min. To this solution was added $ZnCl_2$ (0.26 g) and the reaction mixture was heated to reflux for 12 h. The bulk of the volatiles were removed in vacuo and the residue was poured into 0.5 N $NaHSO_4$ (20 mL). The reaction mixture was extracted with EtOAc (3x 30 mL). The extracts were washed with water (20 mL) and brine (20 mL), combined, dried ($MgSO_4$), filtered, and concentrated. Purification by silica gel chromatography (CH_2Cl_2:MeOH, 60:1 to 15:1 gradient) afforded 22 mg (5%) of Compound **589** as a white solid: R_f 0.19 (15:1 CH_2Cl_2:MeOH); ^{1}H NMR (400 MHz,

acetone-d_6) 11.95 (br s, 1 H), 7.50 (d, J = 7.8, 1 H), 7.02 (d, J = 7.8, 1 H), 6.77 (s, 1 H), 6.63 (s, 1 H), 3.75 (t, J = 4.8, 4 H), 3.25 (t, J = 4.8, 4 H).

EXAMPLE 306

5-Amino-7-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 592, Structure 94 of Scheme XVIII, where R^1 = H, R^2 = chlrorine)

To a solution of 5-chloro-3-phenylenediamine (Structure **92** of Scheme XVIII, where R^1 = H, R^2 = chlorine) (2.5 g, 17.63 mmol) and EtOH (10 mL) was added ethyl 4,4,4-trifluoroacetoacetate (2.7 mL, 17.9 mmol). The dark reaction mixture was heated to reflux under nitrogen. After 15 hrs, the reaction mixture was filtered to afford 3.0 g (61%) of 5-Amino-7-chloro-4-hydroxy-4-trifluoromethyl-3,4-dihydro-2-(1*H*)-quinolinone (Compound **593**, Structure **93** of Scheme XVIII, where R^1 = H, R^2 = chlrorine) as a gray-brown solid: ^{1}H NMR (400 MHz, DMSO-d_6) 10.12 (brs, 1 H), 7.44 (s, 1 H), 6.33 (d, J = 2.1, 1 H), 6.11 (d, J = 2.1, 1 H), 5.86 (s, 2 H), 3.05 (d, J = 16.4, 1 H), 2.69 (d, J = 16.4, 1 H). The filtrate was purified by chromatography (5-50% EtOAc/hex) to afford 100 mg of Compound **592** as a yellow solid: ^{1}H NMR (400 MHz, DMSO-d_6) 11.50 (brs, 1 H), 6.82 (s, 1 H), 6.70 (d, J = 1.8, 1 H), 6.67 (d, J = 1.8, 1 H), 5.68 (s, 2 H).

Compound **593** was converted to Compound **592** by the treatment with an acid.

EXAMPLE 307

5-Propylamino-7-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 594, Structure 96 of Scheme XVIII, where R = propyl, R^1 = H, R^2 = chlrorine)

This compound was prepared in a similar fashion as that described in Example 2, General Procedure IV but using Compound **592** (Structure **94** of Scheme XVIII, where R^1 = H, R^2 = chlrorine) (50 mg, 0.19 mmol) in place of Compound **200**. Compound **594** was isolated in 90% yield as a yellow solid: ^{1}H NMR (400 MHz, CD_3OD) 6.90 (s, 1 H), 6.65 (s, 1 H), 4.99 (brs, 1 H), 3.10 (m, 2 H), 1.62 (q, J = 7.4, 2 H), 1.05 (t, J = 7.4, 3 H).

EXAMPLE 308

7-Chloro-5-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 595, Structure 95 of Scheme XVIII, where R^1 = H, R^2 = chlrorine)

A mixture of Compound **593** (Structure **93** of Scheme XVIII, where R^1 = H, R^2 = chlrorine) (100 mg, 0.36 mmol), water (5 mL), concn. H_2SO_4 (4 mL) and ice (6 g) was cooled to 0 °C. An aqueous solution (1 mL) of sodium nitrite (28 mg, 0.40 mmol) was added dropwise with stirring. The mixture was cautiously poured into 15 mL of boiling (140 °C) 10 M H_2SO_4. The boiling was continued for 10 min. and the mixture was diluted with water and cooled to room temperature to give a yellow/orange precipitate which was filtered and washed with water then dissolved in acetone and concentrated in vacuo to afford 80 mg (84%) of Compound **595** as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.10 (brs, 1 H), 10.25 (brs, 1 H), 7.05 (d, J = 1.8, 1 H), 6.89 (s, 1 H), 6.80 (d, J = 1.8, 1 H).

EXAMPLE 309

5-Amino-6-bromo-3,4-dihydro-4-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 596, Structure 93 of Scheme XVIII, where R^1 = bromine, R^2 = H)

4-Bromophenylenediamine (Compound **597**, Structure **92** of Scheme XVIII, where R^1 = bromine, R^2 = H):

A suspension of 2-bromo-5-nitroaniline (10 g, 46 mmol), zinc dust (15 g, 0.23 mol), and calcium chloride dihydrate (20 g, 0.14 mol) in 140 mL 95% EtOH/water was heated at reflux for 12 h. The mixture was filtered through Celite, washed with hot EtOAc and concentrated to a tan solid. Flash chromatography (50% EtOAc/hexanes) afforded 5.8 g (67%) of Compound **597**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.13 (d, 1H, J = 8.5), 6.12 (d, 1H, J = 2.6), 6.01 (dd, 1H, J = 8.5, 2.6), 3.95 (broad s, 2H), 3.56 (broad s, 2H).

5-Amino-6-bromo-3,4-dihydro-4-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **596**, Structure **93** of Scheme XVIII, where R^1 = bromine, R^2 = H):

To a solution of Compound **597** (5.7 g, 30 mmol) in 100 mL toluene was added ethyl trifluoroacetoacetate (4.9 mL, 34 mmol, 1.1 eq) dropwise. The solution was heated at reflux for 18 h. The solvent was allowed to cool to room temperature, then placed in a refrigerator (0 °C). The solid was filtered and rinsed with cold toluene. Flash chromatography (1:1 EtOAc:dichloromethane) afforded 3.6 g (37%) of Compound **596** as a tan solid: ^{1}H NMR (400

MHz, acetone-d_6) 9.31 (broad s, 1H), 7.37 (d, 1H, J = 8.5), 6.73 (s, 1H), 6.28 (d, 1H, J = 8.5), 5.83 (broad s, 2H), 3.16 (d, AB, 1H, J = 16.9), 2.97 (d, AB, 1H, J = 16.9).

EXAMPLE 310

6-Bromo-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 598, Structure 98 of Scheme XVIII, where R^1 = bromine, R^2 = H)

6-Bromo-5-chloro-3,4-dihydro-4-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **599**, Structure **97** of Scheme XVIII, where R^1 = bromine, R^2 = H):

In a dry flask, to a solution of $CuCl_2$ (2.5 g, 18 mmol, 2 eq) in 60 mL anhydrous acetonitrile was added *t*-butyl nitrite (2.1 mL, 18 mmol, 1.9 eq). The solution turned black. A solution of the aniline (3.0 g, 9.3 mmol) in 150 mL was added via cannula. The mixture was stirred at rt for 3h, then partitioned with EtOAc (200 mL) and water (200 mL). The water layer was extracted with EtOAc (200 mL), washed with sat'd $NaHCO_3$ (100 mL), then brine (100 mL), dried ($MgSO_4$), filtered and concentrated. The crude material was purified by flash chromatography (95:5 hexanes:EtOAc, gradient to 50:50 hexanes:EtOAc) to afford 2.5 g (79%) of Compound **599** as an off-white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 9.74 (broad s, 1H), 7.66 (d, 1H, J = 8.5), 6.82 (d, 1H, J = 8.5), 5.08 (s, 1H), 3.19 (d, AB, 1H, J = 17.2), 3.05 (d, AB, 1H, J = 17.2).

6-Bromo-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **598**, Structure **98** of Scheme XVIII, where R^1 = bromine, R^2 = H):

A solution of Compound **599** (2.5 g, 7.3 mmol) in 22 mL conc. H_2SO_4 was heated at 90 °C for 1 h, whereupon TLC analysis (1:1 EtOAc:hexanes) showed complete consumption of starting material. The reaction was poured over ice, and a white precipitate formed. The solid was filtered and washed with hexanes. The solid was dissolved in hot EtOAc and filtered through Celite to afford 2.2 g (92%) of an off-white solid. ^{1}H NMR (400 MHz, acetone-d_6) 11.4 (broad s, 1H), 7.99 (d, 1H, J = 9.0), 7.49 (d, 1H, J = 9.0), 7.22 (s, 1H).

EXAMPLE 311

6-(bis-N,N-2,2,2-trifluoroethyl)amino-5-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **600**, Structure **100** of Scheme XVIII, where R = methoxy, $R^1 = R^2$ = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 6-amino-5-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **601**, Structure **99** of Scheme XVIII, where R = methoxy) and trifluoroacetic acid. Compound **600** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 12.00-12.20 (bs, 1H), 7.45 (d, J = 8.8, 1H), 7.22 (d, J = 2.9, 1H), 7.20 (s, 1H), 4.02 (q, J = 8.8, 4H), 3.88 (s, 3H).

EXAMPLE 312

6-(N-2,2,2-Trifluoroethyl)amino-5-propyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **602**, Structure **100** of Scheme XVIII, where R = propyloxy, R^1 = H, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 6-amino-5-propyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **603**, Structure **99** of Scheme XVIII, where R = propyloxy) and trifluoroacetic acid. Compound **602** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$) 10.56 (bs, 1H), 7.18 (s, 1H), 4.14 (d, J = 9.6, 1H), 7.11 (d, J = 9.6, 1H), 4.45 (t, J = 6.6, 1H), 3.83 (quin, J = 7.4, 2H), 3.74 (t, J = 6.6, 2H), 1.86 (q, J = 7.3, 2H), 1.07 (t, J = 7.4, 3H).

EXAMPLE 313

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-propyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **604**, Structure **100** of Scheme XVIII, where R = propyloxy, $R^1 = R^2$ = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **603** (Structure **99** of Scheme XVIII, where R = propyloxy) and trifluoroacetic acid. Compound **604** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$) 10.75 (bs, 1H), 7.43 (d, J = 9.0, 1H), 7.19 (s, 1H), 7.17 (d, J = 9.0, 1H), 4.03 (q, J = 8.9, 4H), 3.93 (t, J = 7.1, 2H), 1.83 (q, J = 7.3, 2H), 1.01 (t, J = 7.4, 3H).

EXAMPLE 314

6-(N-2,2,2-Trifluoroethyl)amino-5-ethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 605, Structure 100 of Scheme XVIII, where R = ethoxy, R^1 = H, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 6-amino-5-ethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **606**, Structure **99** of Scheme XVIII, where R = ethoxy) and trifluoroacetic acid. Compound **605** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$) 10.65 (bs, 1H), 7.17 (s, 1H), 7.11 (s, 1H), 4.44 (t, 7.2, 1H), 3.86-3.81 (m, 4H), 1.44 (t, *J* = 6.9, 3H).

EXAMPLE 315

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-ethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 607, Structure 100 of Scheme XVIII, where R = ethoxy, R^1 = R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **606** (Structure **99** of Scheme XVIII, where R = ethoxy) and trifluoroacetic acid. Compound **607** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$) 11.05 (bs, 1H), 7.44 (s, 1H), 7.20 (s, 2H), 4.05 (m, 6H), 1.39 (t, *J* = 6.9, 3H).

EXAMPLE 316

6-(N-2,2,2-Trifluoroethyl)amino-5-(3,3,3-trifluoropropyloxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 608, Structure 100 of Scheme XVIII, where R = 3,3,3-trifluoropropyloxy, R^1 = H, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 6-amino-5-(3,3,3-trifluoropropyloxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **609**, Structure **99** of Scheme XVIII, where R = 3,3,3-trifluoropropyloxy) and trifluoroacetic acid. Compound **608** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$) 11.15 (bs, 1H), 7.92 (d, *J* = 6.7, 1H), 7.72 (d, *J* = 6.7, 1H), 7.59 (m, 2H), 4.23 (m, 2H), 1.67 (m, 2H), 1.41 (m, 2H).

EXAMPLE 317

6-(N-2,2,2-Trifluoroethyl)amino-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **610**, Structure **100** of Scheme XVIII, where R = chloro, R^1 = H, R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from 6-amino-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **611**, Structure **99** of Scheme XVIII, where R = chloro) and trifluoroacetic acid. Compound **610** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$) 11.15 (bs, 1H), 7.38 (d, *J* = 9.1, 1H),7.33 (s, 1H), 7.17 (d, *J* = 9.1, 1H), 5.07 (t, *J* = 8.3, 1H), 3.92 (quin, *J* = 8.5, 2H).

EXAMPLE 318

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **612**, Structure **100** of Scheme XVIII, where R = chloro, R^1 = R^2 = 2,2,2-trifluoroethyl)

This compound was prepared in a similar fashion as that described in Example 9, General Procedure VI from Compound **611** (Structure **99** of Scheme XVIII, where R = chloro) and trifluoroacetic acid. Compound **612** was isolated as yellow solid. ^{1}H NMR ($CDCl_3$) 10.62 (bs, 1H), 7.6 (d, *J* = 8.7, 1H), 7.39 (d, *J* = 8.8, 1H), 7.34 (s, 1H), 3.83 (q, *J* = 8.6, 4H).

EXAMPLE 319

6-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **613**, Structure **102** of Scheme XIX, where R^1 = R^3 = R^4 = H, R^2 = fluorine)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 4-fluoroaniline (Structure **101** of Scheme XIX, where R^3 = R^4 = H, R^2 = fluorine) in place of Compound **200**. Compound **613** was isolated as a white solid: ^{1}H NMR (400 MHz, acetone-d_6) 10.87 (s, 1H), 7.58-7.48 (m, 2H), 7.43 (d, *J* = 9.7, 1H), 7.01 (s, 1H).

EXAMPLE 320

6-Chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **614**, Structure **102** of Scheme XIX, where R^1 = R^3 = R^4 = H, R^2 = chlorine)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 4-chloroaniline (Structure **101** of Scheme XIX, where R^2 = fluorine, R^3 = R^4 = H) in place of Compound **200**. Compound **614** was isolated as a white solid: ^{1}H NMR (400

MHz, acetone-d_6 + drop of DMSO- d_6) 10.90 (s, 1H), 7.68-7.60 (m, 2H), 7.53 (d, J = 9.0, 1H), 7.01 (s, 1H).

EXAMPLE 321

6-Isopropyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **615**, Structure **102** of Scheme XIX, where $R^1 = R^3 = R^4 = H$, R^2 = isopropyl)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 4-isopropylaniline (Structure **101** of Scheme XIX, where R^2 = isopropyl, $R^3 = R^4 = H$) in place of Compound **200**. Compound **615** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 10.60 (s, 1 H), 7.64 (s, 1 H), 7.50 (d, J = 8.1, 1 H), 7.27 (d, J = 8.1, 1 H), 7.06 (s, 1 H), 5.45 (q, J = 5.6, 1 H), 1.43 (d, J = 5.6, 6 H).

EXAMPLE 322

6-Cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **616**, Structure **102** of Scheme XIX, where $R^1 = R^3 = R^4 = H$, R^2 = cyclohexyl)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 4-cyclohexylaniline (Structure **101** of Scheme XIX, where R^2 = cyclohexyl, $R^3 = R^4 = H$) in place of Compound **200**. Compound **616** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.75 (bs, 1 H), 7.62 (s, 1 H), 7.49 (dd, J = 8.4, 1.5, 1 H), 7.42 (d, J = 8.7, 1 H), 7.08 (s, 1 H), 2.60 (bt, 1 H), 1.90 (m, 4 H), 1.78 (m, 1 H), 1.43 (m, 4 H), 1.26 (m, 1 H).

EXAMPLE 323

6-(1- *trans*-Propenyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **617**, Structure **102** of Scheme XIX, where $R^1 = R^3 = R^4 = H$, R^2 = 1-propenyl)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 4-(1-*trans*-propenyl)aniline (Structure **101** of Scheme XIX, where R^2 = 1-*trans*-propenyl, $R^3 = R^4 = H$) in place of Compound **200**. Compound **617** was isolated as a white solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.60 (s, 1H), 7.76 (dd, J = 8.6, 1.6, 1H) 7.65 (s, 1H), 7.48 (d, J = 8.6, 1H), 6.93 (s, 1H), 6.54 (d, J = 15.8, 1H), 6.38-6.32 (m, 1H), 1.88 (dd, J = 6.4, 1.3, 3H).

EXAMPLE 324

6-Cyclohexyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **618**, Structure **102** of Scheme XIX, where R^1 = fluorine, R^2 = cyclohexyl, $R^3 = R^4$ = H)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 4-cyclohexylaniline (Structure **101** of Scheme XIX, where R^2 = cyclohexyl, $R^3 = R^4$ = H) and ethyl 2,4,4,4-tetrafluoroacetoacetate in place of Compound **200** and 4,4,4-trifluoroacetoacetate. Compound **618** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.48 (bs, 1H), 7.49 (m, 2H), 77.38 (d, J = 7.6, 1H), 2.59 (m, 1H), 1.81 (m, 4H), 1.70 (m, 2H), 1.40 (m, 4H).

EXAMPLE 325

7-Fluoro-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **619**, Structure **102** of Scheme XIX, where $R^1 = R^3$ = H, R^2 = methyl, R^4 = fluoro)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 3-fluoro-4-methylaniline (Structure **101** of Scheme XIX, where R^3 = H, R^2 = methyl, R^4 = fluoro) and 4,4,4-trifluoroacetoacetate in place of Compound **200**. Compound **619** was isolated as a white solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.22 (s, 1H), 7.67 (d, J = 7.3, 1H), 7.20 (d, J = 10.6, 1H), 6.86 (s, 1H), 2.35 (d, J = 1.4, 3H).

EXAMPLE 326

5,7-Difluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **620**, Structure **102** of Scheme XIX, where $R^1 = R^2$ = H, $R^3 = R^4$ = fluoro)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 3,5-difluoroaniline (Structure **101** of Scheme XIX, where R^2 = H, $R^3 = R^4$ = fluoro) and 4,4,4-trifluoroacetoacetate in place of Compound **200**. Compound **620** was isolated as a white solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.50 (s, 1H), 7.15 (dd, J = 8.6, 2.5, 1H), 7.13-7.01(m, 2H).

EXAMPLE 327

6-Methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **621**, Structure **102** of Scheme XIX, where $R^1 = R^3 = R^4 = H$, R^2 = methoxy)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I but using 4-methoxyaniline (Structure **101** of Scheme XIX, where R^2 = methoxy, $R^3 = R^4 = H$) and 4,4,4-trifluoroacetoacetate in place of Compound **200**. Compound **621** was isolated as a white solid: ^{1}H NMR (400 MHz, acetone-d_6) 7.50 (d, J = 9.0, 1H), 7.33 (dd, J = 9.0 and 2.5, 1H), 7.19 (d, J = 2.5, 1H), 6.95 (s, 1H), 3.88 (s, 3H).

EXAMPLE 328

6-Benzyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **623**, Structure **104** of Scheme XIX, where R^5 = benzyl)

6-Hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **622**, Structure **103** of Scheme XIX):

To a solution of Compound **621** (Structure **102** of Scheme XIX, where $R^1 = R^3 = R^4 = H$, R^2 = methoxy) (0.20 g, 0.82 mmol) in CH_2Cl_2 was added BBr_3 and the reaction mixture was allowed to stir at rt overnight. The reaction was quenched with H_2SO_4 (1M aqueous), extracted with EtOAc and washed with $NaHCO_3$ (sat. aqueous). Recrystallization afforded Compound **622** (0.17 g , 88%) as a yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.10 (bs, 1H), 8.75 (s, 1H), 7.43 (d, J = 8.7, 1H), 7.30-7.18 (m, 2H), 6.93 (s, 1H).

6-Benzyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **623**, Structure **103** of Scheme XIX, where R^5 = benzyl):

A mixture of Compound **622**, benzyl bromide (1 equiv) and Na_2CO_3 in acetone was stirred at rt overnight. Standard procedure afforded Compound **623** as a white solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.36 (s, 1H), 7.52-7.47 (m, 4H), 7.42-7.22 (m, 4H), 7.27 (s, 1H), 5.21 (s, 2H).

EXAMPLE 329

6-(3-Pentyloxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 624, Structure 104 of Scheme XIX, where R^5 = 3-pentyl)

A mixture of Compound **622** (Structure **103** of Scheme **XVIII**), 3-bromopentane and sodium hydride in DMF was heated at 130 °C for 2h. The reaction was quenched with water and extracted with EtOAc. Removal of solvent followed by chromatography provided Compound **624** as a pale yellow solid: ^{1}H NMR (400 MHz, acetone-d_6) 11.60 (s, 1H), 7.48 (d, J = 9.0, 1H), 7.34 (dd, J = 9.0, 2.5, 1H), 7.21 (s, 1H), 6.97 (s, 1H), 6.94 (s, 1H), 4.26-4.23 (m, 1H), 1.74-1.67 (m, 4H), 0.97 (t, J = 7.4, 6H).

EXAMPLE 330

6-(1-Hydroxy-3,3,5,5-tetramethyl)cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 625, Structure 105 of Scheme XX, where R = R^1 = R^2 = R^5 = R^6 = H, R^3 = R^4 = methyl, n = 1, Z = -CH_2CMe_2-)

This compound was prepared by the following General Procedure XIX (Alkylation of an arylbromide by a ketone):

A solution of an arylbromide in dry THF (0.1-0.5 M) is cooled to –70 °C under a N_2 atmosphere. The aryl bromide is then treated, if needed for amide deprotonation, with MeLi (1.2 equiv) and stirred at –70 °C for 15 min before the addition of *n*-BuLi (1.2 equiv), the reaction mixture was allowed to stir an additional 20 min at –70 °C, warmed to –30 °C, where the dianion is then quenched with a ketone (2.0 equiv). The reaction mixture is then warmed to room temperature overnight, diluted with water and extracted with EtOAc (3x 20 mL/mmol). The combined organic extracts were then washed with Brine (20 mL/mmol), dried ($MgSO_4$), filtered and concentrated. Purification by trituration (EtOAc/hexane, 20%) or recrystallization (MeOH) afforded the desired alcohol.

Compound **625** was prepared from Compound **308** (Structure **16a** of Scheme XX, where R = R^1 = H) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.99 (s, 1 H), 7.73 (d, J = 8.8, 1 H), 7.37 (d, J = 8.8, 1 H), 7.08 (s, 1 H), 2.13 (s, 1 H), 1.61 (m, 4 H), 1.34 (s, 6 H), 1.26 (m, 2 H), 0.97 (s, 6 H).

EXAMPLE 331

6-(3,3,5,5-Tetramethyl)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 626, Structure 106 of Scheme XX, where $R = R^1 = R^2 = R^5 = R^6 = H$, $R^3 = R^4 =$ methyl, n = 1, Z = $-CH_2CMe_2-$)

This compound was prepared by the following General Procedure XX (Dehydration of an alcohol):

A solution of the benzylic alcohol, such as Compound **625** (Structure **105** of Scheme XX, where $R = R^1 = R^2 = R^5 = R^6 = H$, $R^3 = R^4 =$ methyl, n = 1, Z = $-CH_2CMe_2-$), in CH_2Cl_2 (0.1M) is treated with trifluoroacetic acid (excess) or TsOH and stirred for 2 h at room temperature. The reaction mixture is then poured into cool saturated $NaHCO_3$ solution and the pH adjusted to pH 7. The reaction solution is then partitioned and the aqueous layer is extracted with CH_2Cl_2 (3 x 15 mL/mmol). The combined organic layers are then washed with water (10 mL/mmol), Brine (10mL/mmol), dried ($MgSO_4$), filtered and concentrated to give crude olefin product. Purification by recrystallization (MeOH/EtOAc) gives pure olefin product in good yield.

Compound **626** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.74 (s, 1 H), 7.67 (d, J = 8.0, 1 H), 7.42 (d, J = 8.0, 1 H), 7.11 (s, 1 H), 5.83 (s, 1 H), 2.23 (s, 2 H), 1.44 (s, 2 H), 1.12 (s, 6 H), 1.06 (s, 6 H).

EXAMPLE 332

6-(5,5-Dimethycyclopentenyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 627, Structure 106 of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6 =$ methyl, n = 1, Z = methylene)

This compound was prepared in a similar fashion as that described in Examples 330 and 331, General Procedures XIX and XX but using 2,2-dimethylcyclopentanone in place of 3,3,5,5-tetramethylcyclohexanone. Compound **627** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.80 (s, 1 H), 7.60 (d, J = 8.0, 1 H), 7.39 (d, J = 8.0, 1 H), 7.11 (s, 1 H), 5.85 (t, J = 4.0, 1 H), 2.41 (td, J = 4.0, J = 8.0, 2 H), 1.90 (t, J = 8.0, 2 H), 1.23 (s, 6 H).

EXAMPLE 333

(±)-6-(2,2-Dimethycyclopentyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **628**, Structure **107** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = methyl, n = 1, Z = methylene)

This compound was prepared in a similar fashion as that described in Example 1 General Procedure III from Compound **627** (Structure **106** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = H$, $R^5 = R^6$ = methyl, n = 1, Z = methylene). Compound **628** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 11.25 (br s, 1 H), 7.62 (s, 1 H), 7.45 (d, *J* = 8.0, 1 H), 7.30 (d, *J* = 8.0, 1 H), 7.07 (s, 1 H), 2.79 (t, *J* = 8.0, 2 H), 2.06 (m, 2 H), 1.86 (m, 2 H), 1.62 (m, 2 H), 1.00 (s, 3 H), 0.62 (s, 3 H).

EXAMPLE 334

6-(1-Hydroxycyclohexyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **629**, Structure **105** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = H$, n = 2, Z = methylene)

This compound was prepared according to General Procedure XIX in Example 330 from Compound **308** (Structure **16a** of Scheme XX, where $R = R^1 = H$) (1.0 g, 3.4 mmol) and cyclohexanone (0.71 mL, 6.8 mmol) to yield 485 mg (46%) of Compound **629** as a white solid: ^1H NMR (400 MHz, DMSO-d_6) 12.26 (s, 1 H), 7.88 (s, 1 H), 7.75 (dd, *J* = 8.7, 1.5, 1 H), 7.38 (d, *J* = 8.6, 1 H), 6.96 (s, 1 H), 4.91 (s, 1 H), 1.77-1.62 (mm, 8 H), 1.59-1.49 (m, 2 H).

EXAMPLE 335

6-Cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **630**, Structure **106** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = H$, n = 2, Z = methylene)

Compound **630** was prepared according to General Procedure XX in Example 331 by dehydration of Compound **629** (Structure **105** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = H$, n = 2, Z = methylene) (1.0g, 3.4 mmol) in 83% yield as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 11.07 (bs, 1 H), 7.77 (s, 1 H), 7.65 (dd, *J* = 8.4, 1.5, 1 H), 7.29 (d, *J* = 8.6, 1 H), 7.07 (s, 1 H), 6.17 (bt, 1 H), 2.43 (m, 2 H), 2.25 (m, 2 H), 1.81 (m, 2 H), 1.68 (m, 2 H).

EXAMPLE 336

6-Cyclohexyl-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **631**, Structure **108** of Scheme XX, where $R^4 = R^5 = H$, n = 2, Z = methylene)

In 10-mL r.b. flask, a solution of Compound **616** (Structure **107** of Scheme XX, where R = R^{1-6} = H, n = 2, Z = methylene) (39 mg, 0.13 mmol) in toluene (2 mL) was treated with Lawsson's reagent (66 mg, 0.16 mmol, 1.2 equiv). The reaction mixture was then stirred at room temperature overnight, diluted with EtOAc (80 mL), washed with sat. $NaHCO_3$ (15 mL), water (15 mL), Brine (15 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield crude product. Purification by column chromatography (15% EtOAc/hexane) afforded 30 mg (73%) of Compound **631** as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.82 (bs, 1 H), 7.71 (s, 1 H), 7.65 (s, 1 H), 7.53 (dd, J = 8.6, 1.6, 1 H), 7.39 (d, J = 8.6, 1 H), 2.62 (bs, 1 H), 1.89-1.76 (mm, 6 H), 1.45-1.40 (m, 4 H).

EXAMPLE 337

6-Cyclopentenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **632**, Structure **106** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = H$, n = 1, Z = methylene)

This compound was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **308** (Structure **16a** of Scheme XX, where $R = R^1 = H$) (50 mg, 0.17 mmol) and cyclopentanone (0.02 mL, 0.26 mmol) to yield 15 mg (31%) of Compound **632** as white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.36 (bs, 1 H), 7.88 (dd, J = 8.7, 1.4, 1 H), 7.55 (s, 1 H), 7.41 (d, J = 8.7, 1 H), 6.99 (s, 1 H), 6.33 (bm, 1 H), 2.68 (m, 2 H), 2.51 (m, 2 H), 1.99 (m, J = 6.6, 2 H).

EXAMPLE 338

6-Cycloheptenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **633**, Structure **106** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = H$, n = 3, Z = methylene)

Compound **633** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **308** (Structure **16a** of Scheme XX, where $R = R^1 = H$) and cycloheptanone as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.31 (s, 1 H), 7.63 (d, J = 8.7, 1 H), 7.51 (s, 1 H), 7.39 (d, J = 8.6, 1 H), 6.98 (s, 1 H), 6.11 (t, J = 6.7, 1 H), 2.57 (m, 2 H), 2.29 (m, 2 H), 1.80 (m, 2 H), 1.60 (m, 2 H), 1.51 (m, 2 H).

EXAMPLE 339

6-Bromo-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **634**, Structure **16a** of Scheme XX, where R = fluorine, R^1 = H)

In a 100-mL flask a solution of 4-bromoaniline (20g, 116mmol) and ethyl-4,4,4-trifluoroacetoacetate (25.5 mL, 175 mmol, 1.5 equiv) in toluene (5 mL) is heated to reflux for 5 h, cooled and excess solvent removed to provide N-(4-bromophenyl)-4,4,4-trifluoroacetoacetamide (Structure **15** of Scheme XX). The crude reaction mixture is then dissolved in CH_2Cl_2 (40 mL) and water (10 mL) and then treated with *N*-fluorobenzenesulfonimide (1.1 equiv) at room temperature overnight. The reaction mixture is then diluted with water (30 mL) and partitioned. The aqueous layer is extracted with CH_2Cl_2 (3 x 75 mL), the combined organic layers are then washed with sat $NaHCO_3$ (25 mL), saturated NH_4Cl (2 x 25 mL), water (25 mL), Brine (25 mL), dried ($MgSO_4$), filtered and concentrated to afford N-(4-bromophenyl)-2,4,4,4-tetrafluoroacetoacetamide (Structure **15a** of Scheme XX). The crude product was then dissolved in concentrated H_2SO_4 (10 mL) and heated to 80 °C for 3-4 h, cooled to room temperature, and poured over NaOH pellets/ice. The cold aqueous solution was then filtered, the white precipitate was then redissolved in EtOAc (200 mL), washed with water (2 x 20 mL), Brine (25 mL), dried ($MgSO_4$), filtered and concentrated to yield Compound **634** as a white powder: ^{1}H NMR (400 MHz, DMSO-d_6) 12.92 (bs, 1 H), 7.83 (dd, J = 8.0, 1.2, 1 H), 7.77 (s, 1 H), 7.41 (d, J = 7.9, 1 H).

EXAMPLE 340

6-Cyclohexenyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **635**, Structure **106** of Scheme XX, where R = fluorine, $R^1 = R^2 = R^3 = R^4 = R^5 = R^6$ = H, n = 2, Z = methylene)

Compound **635** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **634** (Structure **16a** of Scheme XX, where R = fluorine, R^1 = H) (50 mg, 0.16 mmol) and cyclohexanone (0.030 mL, 0.24 mmol) as a white solid in 20% yield: ^{1}H NMR (400 MHz, DMSO-d_6) 12.80 (s, 1 H), 7.72 (d, J = 8.7, 1 H), 7.59 (s, 1 H), 7.38 (d, J = 8.6, 1 H), 6.18 (s, 1 H), 2.37 (m, 2 H), 2.19 (m, 2 H), 1.74 (m, 2 H), 1.62 (m, 2 H).

EXAMPLE 341

6-Cyclohexyl-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **636**, Structure **107** of Scheme XX, where R = R^2 = R^3 = R^4 = R^5 = R^6 = H, R^1 = methoxy, n = 2, Z = methylene)

6-Bromo-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **637**, Structure **16a** of Scheme XX, where R = H, R^1 = methoxy):

To a 100-mL r.b. flask containing Compound **419** (Structure **29a** of Scheme XX) (1.0 g, 4.11 mmol) in DMF (40 mL) was added, in portions, NBS (0.84 g, 4.73 mmol, 1.15 equiv). The reaction was allowed to stir overnight and poured into water (25 mL), the resulting precipitate was collected by vacuum filtration to yield 1.0 g (76%) of Compound **637**: ^{1}H NMR (400 MHz, DMSO-d_6) 12.31 (bs, 1 H), 7.76 (s, 1 H), 7.06 (s, 1 H), 6.87 (s, 1 H), 3.93 (s, 3 H).

6-Cyclohexyl-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **636**, Structure **107** of Scheme XX, where R = R^2 = R^3 = R^4 = R^5 = R^6 = H, R^1 = methoxy, n = 2, Z = methylene):

This compound is prepared according to General Procedures XIX, XX, and III in Examples 330, 331 and 1 from Compound **637** (350 mg) and cyclohexanone as a white solid in 38% yield: ^{1}H NMR (400 MHz, DMSO-d_6) 12.17 (bs, 1 H), 7.30 (s, 1 H), 6.95 (s, 1 H), 6.78 (s, 1 H), 5.71 (bs, 1 H), 3.84 (s, 3 H), 2.28 (m, 2 H), 2.14 (m, 2 H), 1.67-1.63 (m, 4 H).

EXAMPLE 342

6-Cyclopentyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **638**, Structure **107** of Scheme XX, where R = fluorine, R^1 = R^2 = R^3 = R^4 = R^5 = R^6 = H, n = 1, Z = methylene)

Compound **638** was made according to General Procedures XIX, XX, and III in Examples 330, 331 and 1 from Compound **634** (Structure **16a** of Scheme XX, where R = fluorine, R^1 = H) and cyclopentanone as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 7.53 (m, 2H), 7.38 (d, J = 8.4, 1H), 3.07 (quint., J = 8.2, 1H), 2.03 (m, 2H), 1.78 (m, 2H), 1.66 (m, 2H), 1.53 (m, 2H).

EXAMPLE 343

(Z)-6-(1-Propyl-1-butenyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **639**, Structure **106** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^5 = H$, R^4 = methyl, R^6 = ethyl, n = 1, Z = two no-bond hydrogens) and (E)-6-(1-Propyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **640**, Structure **106** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^5 = H$, R^4 = methyl, R^6 = ethyl, n = 1, Z = two no-bond hydrogens)

Compounds **639** and **640** were made according to General Procedures Procedures XIX and XX in Examples 330 and 331 from Compound **308** (Structure **16a** of Scheme XX, where $R = R^1 = H$) and 3-hexanone as a 1/2 mixture of E/Z isomers, Z-isomer: ^1H NMR (400 MHz, $CDCl_3$) 11.10 (s, 1 H), 7.74 (s, 1 H), 7.60 (d, *J* = 8.6, 1.5, 1 H), 7.40 (d, *J* = 8.6, 1 H), 7.06 (s, 1 H), 5.70 (t, *J* = 7.2, 1 H), 2.50 (t, *J* = 7.4, 2 H), 2028-2.20 (m, 2 H), 1.46-1.13 (m, 2 H), 1.00 (t, *J* = 7.5, 3 H), 0.88 (t, *J* = 7.3, 3 H); E-isomer: ^1H NMR (400 MHz, $CDCl_3$) 11.10 (s, 1 H), 7.58 (s, 1 H), 7.40 (d, *J* = 8.2, 1 H), 7.32 (d, *J* = 8.2, 1 H), 7.06 (s, 1 H), 5.53 (t, *J* = 6.9, 1 H), 2.33 (t, *J* = 7.5, 2 H), 1.96-1.78 (m, 2 H), 1.46-1.31 (m, 2 H), 0.96 (t, *J* = 7.4, 3 H), 0.87 (t, *J* = 7.3, 3 H).

EXAMPLE 344

6-(1-Propyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **641**, Structure **107** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^5 = H$, R^4 = methyl, R^6 = ethyl, n = 1, Z = two no-bond hydrogens)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compounds **639** and **640** (Structure **106** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^5 = H$, R^4 = methyl, R^6 = ethyl, n = 1, Z = two no-bond hydrogens). Compound **641** was isolated as white solid: ^1H NMR (400 MHz, $CDCl_3$) 11.24 (s, 1 H), 7.55 (s, 1 H), 7.41 (d, *J* = 8.5, 1 H), 7.28 (d, *J* = 8.5, 1 H), 7.07 (s, 1 H), 2.65-2.60 (m, 1 H), 1.69-1.51 (m, 4 H), 1.22-1.10 (m, 4 H), 0.85 (t, *J* = 7.3, 6 H).

EXAMPLE 345

(E)-6-(1-Methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **642**, Structure **106** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = R^5 = H$, R^6 = ethyl, n = 1, Z = two no-bond hydrogens) and (Z)-6-(1-Methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **643**, Structure **106** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = R^5 = H$, R^6 = ethyl, n = 1, Z = two no-bond hydrogens)

Compounds **642** and **643** were made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **308** (Structure **16a** of Scheme XX, where $R = R^1 = H$) and 2-pentanone as a 5/2 mixture of E/Z isomers: *E*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) 10.97 (s, 1 H), 7.78 (s, 1 H), 7.67 (d, *J* = 8.5, 1 H), 7.28 (d, *J* = 8.5, 1 H), 7.07 (s, 1 H), 5.81 (t, *J* = 7.2, 1 H), 2.25 (m, 2 H), 2.10 (s, 3 H), 1.09 (t, *J* = 7.6, 3 H); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) 11.43 (s, 1 H), 7.64 (d, *J* = 1.3, 1 H), 7.46 (dd, *J* = 8.6, 1.3, 1 H), 7.33 (d, *J* = 8.6, 1 H), 7.08 (s, 1 H), 5.56 (t, *J* = 7.4, 1 H), 2.06 (s, 3 H), 2.01-1.94 (m, 2 H), 0.96 (t, *J* = 7.4, 3 H).

EXAMPLE 346

(±)-6-(1-Methyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **644**, Structure **107** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = R^5 = H$, R^6 = ethyl, n = 1, Z = two no-bond hydrogens)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compounds **642** and **643** (Structure **106** of Scheme XX, where $R = R^1 = R^2 = R^3 = R^4 = R^5 = H$, R^6 = ethyl, n = 1, Z = two no-bond hydrogens). Compound **644** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.40 (s, 1 H), 7.26 (s, 1 H), 7.45 (d, *J* = 8.5, 1 H), 7.33 (d, *J* = 8.5, 1 H), 7.07 (s, 1 H), 2.82-2.78 (m, 1 H), 1.58 (q, *J* = 7.7, 2 H), 1.25 (d, *J* = 4.1, 3 H), 1.20-1.10 (m, 2 H), 0.88 (t, *J* = 7.2, 3 H).

EXAMPLE 347

(E)-6-(1-Ethyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **645**, Structure **106** of Scheme XX, where R = R^1 = R^2 = R^3 = R^4 = R^5 = H, R^6 = methyl, n = 1, Z = two no-bond hydrogens) and (Z)-6-(1-Ethyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **646**, Structure **106** of Scheme XX, where R = R^1 = R^2 = R^3 = R^4 = R^5 = H, R^6 = methyl, n = 1, Z = two no-bond hydrogens)

Compounds **645** and **646** were made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **308** (Structure **16a** of Scheme XX, where R = R^1 = H) and 3-pentanone as a 2/3 mixture of E/Z isomers: *E*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) 11.10 (s, 1 H), 7.62-7.59 (m, 1 H), 7.42 (d, *J* = 8.8, 1 H), 7.33 (d, *J* = 8.8, 1 H), 7.08 (s, 1 H), 5.77 (q, *J* = 7.1, 1 H), 2.55 (q, *J* = 7.8, 2 H), 1.83 (d, *J* = 7.1, 3 H), 1.02 (m, 3 H); *Z*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$) 11.10 (s, 1 H), 7.75 (s, 1 H), 7.42 (d, *J* = 8.8, 1 H), 7.33 (d, *J* = 8.8, 1 H), 7.07 (s, 1 H), 5.63 (q, *J* = 6.9, 1 H), 2.38 (q, *J* = 7.8, 2 H), 1.52 (d, *J* = 7.1, 3 H), 1.02 (m, 3 H).

EXAMPLE 348

6-(1-Ethylpropyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **647**, Structure **107** of Scheme XX, where R = R^1 = R^2 = R^3 = R^4 = R^5 = H, R^6 = methyl, n = 1, Z = two no-bond hydrogens)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compounds **645** and **646** (Structure **106** of Scheme XX, where R = R^1 = R^2 = R^3 = R^4 = R^5 = H, R^6 = methyl, n = 1, Z = two no-bond hydrogens). Compound **476** was isolated as white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 12.01 (s, 1 H), 7.56 (s, 1 H), 7.41 (dd, *J* = 8.3, 1.5, 1 H), 7.39 (d, *J* = 8.3, 1 H), 7.08 (s, 1 H), 2.87-2.68 (m, 1 H), 1.52-1.25 (m, 4 H), 0.78 (t, *J* = 7.3, 6 H).

EXAMPLE 349

6-(1-Isopropyl-2-methyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **648**, Structure **106** of Scheme XX, where R = R^1 = R^3 = R^4 = H, R^2 = R^5 = R^6 = methyl, n = 1, Z = two no-bond hydrogens)

Compound **648** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **308** (Structure **16a** of Scheme XX, where R = R^1 = H) and 2,4-

dimethyl-3-pentanone as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.10 (s, 1 H), 7.47 (d, J = 8.4, 1 H), 7.45 (s, 1 H), 7.27 (d, J = 8.4, 1 H), 7.11 (s, 1 H), 3.12-3.07 (m, 1 H), 1.85 (s, 3 H), 1.38 (s, 3 H), 0.88 (d, J = 6.8, 6 H).

EXAMPLE 350

6-(1-Isopropyl-2-methyl)propyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **649**, Structure **107** of Scheme XX, where R = R^1 = R^3 = R^4 = H, R^2 = R^5 = R^6 = methyl, n = 1, Z = two no-bond hydrogens)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compound **648** (Structure **106** of Scheme XX, where R = R^1 = R^3 = R^4 = H, R^2 = R^5 = R^6 = methyl, n = 1, Z = two no-bond hydrogens). Compound **649** was isolated as white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.10 (s, 1 H), 7.52 (s, 1 H), 7.36 (d, J = 8.5, 1 H), 7.31 (d, J = 8.5, 1 H), 7.07 (s, 1 H), 2.21-2.15 (m, 3 H), 0.87 (d, J = 6.5, 6 H), 0.74 (d, J = 6.5, 6 H).

EXAMPLE 351

(Z)-6-(1-Isobutyl-3-methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **650**, Structure **106** of Scheme XX, where R = R^1 = R^2 = R^5 = H, R^3 = R^4 = methyl, R^6 = isopropyl, n = 1, Z = two no-bond hydrogens) and (E)-6-(1-Isobutyl-3-methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **651**, Structure **106** of Scheme XX, where R = R^1 = R^2 = R^5 = H, R^3 = R^4 = methyl, R^6 = isopropyl, n = 1, Z = two no-bond hydrogens)

Compound **650** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **308** (Structure **16a** of Scheme XX, where R = R^1 = H) and 2,6-dimethyl-4-heptanone as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.10 (s, 1 H), 7.58 (s, 1 H), 7.40 (s, 2 H), 7.09 (s, 1 H), 5.31 (d, J = 10.1, 1 H), 2.32-2.24 (m, 1 H), 2.24 (d, J = 7.2, 2 H), 1.49-1.44 (m, 1 H), 0.94 (d, J = 6.6, 6 H), 0.84 (d, J = 6.6, 6 H).

Compound **651** was also isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.10 (s, 2 H), 7.73 (s, 1 H), 7.62 (s, 1 H), 7.11 (s, 1 H), 5.53 (d, J = 9.6, 1 H), 2.78-2.69 (m, 1 H), 2.44 (d, J = 7.2, 2 H), 1.60-1.51 (m, 1 H), 1.06 (d, J = 6.6, 6 H), 0.84 (d, J = 6.6, 6 H).

EXAMPLE 352

6-(1-Isobutyl-3-methyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **652**, Structure **107** of Scheme XX, where R = R^1 = R^2 = R^5 = H, R^3 = R^4 = methyl, R^6 = isopropyl, n = 1, Z = two no-bond hydrogens)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compound **650** (Structure **106** of Scheme XX, where R = R^1 = R^2 = R^5 = H, R^3 = R^4 = methyl, R^6 = isopropyl, n = 1, Z = two no-bond hydrogens). Compound **652** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.31 (s, 1 H), 7.56 (s, 1 H), 7.41 (d, *J* = 8.2, 1 H), 7.35 (d, *J* = 8.2, 1 H), 7.04 (s, 1 H), 2.82-2.78 (m, 1 H), 1.55-1.38 (m, 4 H), 1.32-1.25 (m, 2 H), 0.86 (d, *J* = 6.4, 6 H), 0.81 (d, *J* = 6.4, 6 H).

EXAMPLE 353

6-(1-Propyl)butyl-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **653**, Structure **108** of Scheme XX, where R^4 = R^5 = methyl, n = 1, Z = two no-bond hydrogens)

This compound was prepared in a similar method as that described in Example 95, General Procedure XI but using Compound **641** (Structure **107** of Scheme XX, where R = R^1 = R^2 = R^3 = R^5 = H, R^4 = methyl, R^6 = ethyl, n = 1, Z = two no-bond protons) in place of Compound **209**. Compound **653** was isolated as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.91 (s, 1 H), 7.76 (s, 1 H), 7.69 (s, 1 H), 7.48 (d, *J* = 8.5, 1 H), 7.41 (d, *J* = 8.5, 1 H), 2.69-2.63 (m, 1 H), 1.73-1.51 (m, 4 H), 1.21-1.04 (m, 4 H), 0.82 (t, *J* = 7.2, 6 H).

EXAMPLE 354

6-(3-Oxo-1-)cyclopentenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **654**, Structure **109** of Scheme XXI, where R = H, R^1 = trifluoromethyl, n = 0)

Compound **654** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **308** (Structure **16b** of Scheme XXI, where R = H) and 3-ethoxy-2-cyclopentenone as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.06 (s, 1 H), 8.07 (s, 1 H), 7.91 (d, *J* = 8.6, 1 H), 7.46 (d, *J* = 8.8, 1 H), 7.14 (s, 1 H), 6.64 (s, 1 H), 3.18-3.10 (m, 2 H), 2.70-2.53 (m, 2 H).

EXAMPLE 355

6-(3-Oxo-1-)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **655**, Structure **109** of Scheme XXI, where R = H, R^1 = trifluoromethyl, n = 1)

Compound **655** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **308** (Structure **16b** of Scheme XXI, where R = H) and 3-ethoxy-2-cyclohexenone as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.06 (s, 1 H), 7.97 (s, 1 H), 7.79 (d, *J* = 8.7, 1 H), 7.47 (d, *J* = 8.7, 1 H), 7.13 (s, 1 H), 6.47 (s, 1 H), 2.85-2.81(m, 2 H), 2.54-2.51 (m, 2 H), 2.27-2.21 (m, 2 H), 2.27-2.21 (m, 2 H).

EXAMPLE 356

6-(3-Oxo-1-)cyclopentenyl-3-methyl-4-difluoromethyl-2(1*H*)-quinolinone (Compound **656**, Structure **109** of Scheme XXI, where R = methyl, R^1 = difluoromethyl, n = 0)

To a suspension of Compound **308** (Structure **16b** of Scheme XXI, where R = H) (250 mg, 0.90 mmol) in THF (4 mL) at –40 ^{0}C, MeLi 1.4 M in ether (1.5 equiv) was added followed by *n*-BuLi 1.6 M in hexane (1.1 equiv). A solution of 3-ethoxy-2-cyclopentenone (1.1 equiv) in THF (3 mL) was slowly added to this thick suspension via canula. The mixture was allowed to worm up slowly to room temperature and was allowed to stir over night. The reaction was quenched by HCl 10% until PH~1 then the organic layer was taken into EtOAC (3 x 20 mL), washed with brine (20 mL), and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was crystallized out from EtOAc/EtOH. The resulting cake was further purified by HPLC reverse phase ($MeOH/H_2O/Et_3N$: 60/40/0.5) to give Compound **656** as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 11.20 (s, 1 H), 8.24 (d, *J* = 1.6, 1 H), 7.99 (dd, *J* = 1.6, 8.6, 1 H), 7.67 (t, *J* = 5.1, 1 H), 7.43 (d, *J* = 8.6, 1 H), 6.71 (d, *J* = 1.3, 1 H), 3.06-3.01 (m, 2 H), 2.48-2.43 (m, 2 H), 2.29 (s, 3 H).

EXAMPLE 357

6-(3-Oxo-1-)cyclohexenyl-3-mehyl-4-difluoromethyl-2(1*H*)-quinolinone (Compound **657**, Structure **109** of Scheme XXI, where R = methyl, R^1 = difluoromethyl, n = 1)

This compound was prepared in a similar fashion as that described in Example 356 but using 3-ethoxy-2-cyclohexenone in place of 3-ethoxy-2-cyclopentenone. Compound **657** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 10.15 (s, 1 H), 8.24 (s, 1 H), 7.70 (d, *J* =

9.1, 1 H), 7.27 (d, J = 9.1, 1 H), 7.17 (t, J = 5.9, 1 H), 6.48 (s, 1 H), 2.85-2.78 (m, 2 H), 2.55-2.49 (m, 2 H), 2.42 (s, 3 H), 2.24-2.18 (m, 2 H).

EXAMPLE 358

(±)-6-(3-Hydroxy-1-)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **658**, Structure **110** of Scheme XXI, where R = H, R^1 = trifluoromethyl, n = 1)

This compound was prepared by the following General Procedure XXI (Reduction of ketone):

To a solution of a ketone in dry THF (0.1-0.5 M) at –78 °C was added a 2 equiv of 1.5 M DIBAL/toluene solution. After 30 min., the reaction mixture was quenched with saturated NH_4Cl and extracted with EtOAc. The organic layer was washed with H_2O (3 x) and brine (3 x), dried (Na_2SO_4) and concentrated *in vacuo*. Purification by flash chromatography afforded the alcohol as a white solid in good yield.

Compound **658** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 11.20 (s, 1 H), 7.77 (dd, J = 8.8, 1.4, 1 H), 7.62 (d, J = 1.4, 1 H), 7.41 (d, J = 8.8, 1 H), 6.99 (s, 1 H), 6.10 (s, 1 H), 4.82 (d, J = 5.5, 2 H), 2.37-2.27 (m, 2 H), 1.90-1.87 (m, 2 H), 1.71-1.65 (m, 1 H), 1.53-1.44 (m, 1 H).

EXAMPLE 359

6-(1-Hydroxy-1,1-diphenyl)methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **659**, Structure **111** of Scheme XXII)

Compound **659** was made according to General Procedures XIX in Examples 330 from Compound **308** (Structure **16** of Scheme XXII) and benzophenone as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 10.89 (s, 1 H), 7.78 (d, J = 1.8, 1 H), 7.61 (dd, J = 8.5, 1.8, 1 H), 7.42 (d, J = 8.5, 1 H), 7.37-7.28 (m, 10 H), 7.04 (s, 1 H), 3.02 (s, 1 H).

EXAMPLE 360

6-Diphenylmethyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **660**, Structure **112** of Scheme XXII)

To a solution of Compound **659** (Structure **111** of Scheme XXII) in dichloroethane was added an excess of TFA followed by an excess of triethylsilane. This mixture was allowed to stir over night at room temperature. Quenched by water the organic layer was taken into EtOAc

washed with brine, dried over Na_2SO_4. The solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography to yield Compound **660** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.10 (s, 1 H), 7.55 (s, 1 H), 7.41 (d, J = 8.5, 1 H), 7.35-7.24 (m, 10 H), 7.33 (d, J = 7.1, 4 H), 7.04 (s, 1 H), 5.63 (s, 1 H).

EXAMPLE 361

6-(3-hydroxy-3-methyl-1-)butynyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **661**, Structure **113** of Scheme XXII)

To a solution of Compound **308** (Structure **16** of Scheme XXII) (26 mg, 0.090 mmol), triphenylphosphine (152 mg, 0.06 mmol), CuI (4.2 mg, 0.02 mmol), 2-methyl-2-butynol (8.5 mg, 0.10 mmol) in triethylamine (1 mL) was added $PdCl_2$ (0.2 mg, 0.001 mmol) and the reaction mixture was heated at reflux for 20 min. Pyridine (0.3 mL) was added and the reaction was heated for additional hour. The reaction was quenched with 2 N HCl (20 mL), extracted with EtOAc (20 mL), and concentrated. Removal of solvent and chromatography of the crude residue afforded Compound **661** in 60% yield as a white solid: ^{1}H NMR (500 MHz,DMSO-d_6) 12.5 (bs, 1 H), 7.62 (d, J = 8.8, 1 H), 7.59 (s, 1 H), 7.41 (d, J = 8.8, 1 H), 7.04 (s, 1 H), 5.49 (s, 1 H), 1.46 (s, 6 H).

EXAMPLE 362

6-(1-Hydroxy)cyclopentyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **662**, Structure **115** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 1, Z = methylene)

6-Bromo-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **663**, Structure **114** of Scheme XXIII):

To a solution of Compound **486** (Structure **49a** of Scheme XXIII) (0.46 g, 2.6 mmol) and CCl_4 (20 mL) was added bromine (0.13 mL). Stirred at room temperature for 1.5 hrs. The reaction mixture was concentrated in vacuo to afford an orange solid. Washed solid with hot hexane and filtered to afford 0.61 g of Compound **663** in 91% yield as a light orange solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.03 (br s, 1 H), 7.37 (dd, J = 1.9, 8.3, 1 H), 7.26 (d under solvent peak, 1 H), 6.69 (d, J = 8.3, 1 H), 1.71 (s, 6 H).

6-(1-Hydroxy)cyclopentyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **662**, Structure **115** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 1, Z = methylene):

Compound **662** was prepared according to General Procedure XIX in Example 330 from Compound **663** (50 mg, 0.20 mmol) and cyclopentanone (0.02 mL, 0.24 mmol) in 44% yield (23 mg) as a white solid: ^1H NMR (400 MHz, CD_3OD) 7.36 (d under dd, 2 H), 6.83 (d , J = 8.0, 1 H), 5.48 (s, 1 H), 1.95 (m, 6 H), 1.83 (m, 2 H), 1.67 (s, 6 H).

EXAMPLE 363

6-(1-Cyclopentenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound 664, Structure 116 of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 1, Z = methylene)

This compound was prepared in a similar fashion as that described in Example 331, General Procedure XX from Compound **662** (Structure **115** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 1, Z = methylene). Compound **664** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 8.14 (br s, 1 H), 7.30 (dd, J = 1.4, 8.3, 1 H), 7.18 (d, J = 1.4, 1 H), 6.75 (d, J = 8.3, 1 H), 6.12 (m, 1 H), 2.67 (m, 2 H), 2.53 (m, 2 H), 2.02 (quintet, J = 7.3, 2 H), 1.73 (s, 6 H).

EXAMPLE 364

6-Cyclopentyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound 665, Structure 118 of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 1, Z = methylene)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compound **664** (Structure **116** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 1, Z = methylene). Compound **665** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 8.79 (br s, 1 H), 7.09 (d, J = 8.1, 1 H), 6.97 (s, 1 H), 6.77 (d, J = 8.1, 1 H), 2.95 (m, 1 H), 2.05 (m, 2 H), 1.80 (m, 2 H), 1.69 to 1.62 (m, 10 H).

EXAMPLE 365

6-(1-Hydroxy)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **666**, Structure **115** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 2, Z = methylene)

This compound was prepared according to General Procedure XIX in Example 330 from Compound **663** (Structure **114** of Scheme XXIII) and cyclohexanone as a white solid; ^1H NMR (400 MHz, $CDCl_3$) 7.33 (m, 2 H), 6.72 (d, J = 8.6, 1 H), 1.76 to 1.60 (m, 16 H).

EXAMPLE 366

6-(1-Cyclohexenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **667**, Structure **116** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 2, Z = methylene)

This compound was prepared in a similar fashion as that described in Example 331, General Procedure XX by dehydration of Compound **666** (Structure **115** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 2, Z = methylene). Compound **667** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 7.49 (br s, 1 H), 7.24 (dd, J = 1.4, 8.2, 1 H), 7.14 (d, J = 1.4, 1 H), 6.70 (d, J = 8.2, 1 H), 6.05 (m, 1 H), 2.36 (m, 2 H), 2.20 (m, 2 H), 1.79 to 1.76 (m, 2 H), 1.72 (s, 6 H), 1.67 to 1.60 (m, 2 H).

EXAMPLE 367

6-Cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **668**, Structure **118** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 2, Z = methylene)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compound **667** (Structure **116** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 2, Z = methylene). Compound **668** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 8.61 (br s, 1 H), 7.10 (dd, J = 1.4, 8.2, 1 H), 6.93 (d, J = 1.4, 1 H), 6.78 (d, J = 8.2, 1 H), 2.45 (m, 1 H), 1.98 (m, 5 H), 1.71 (s, 6 H), 1.38 to 1.20 (m, 5 H).

EXAMPLE 368

6-(1-Hydroxycycloheptyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **669**, Structure **115** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 3, Z = methylene)

This compound was prepared according to General Procedure XIX in Example 330 from Compound **663** (Structure **114** of Scheme XXIII) and cycloheptanone as a white solid: ^1H NMR

(400 MHz, $CDCl_3$) 8.90 (br s, 1 H), 7.31 (d under dd, 2 H), 6.80 (d, J = 8.7, 1 H), 2.04 (m, 2 H), 1.80 (m, 2 H), 1.78 to 1.56 (m, 14 H).

EXAMPLE 369

6-(1-Cycloheptenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **670**, Structure **116** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 3, Z = methylene)

This compound was prepared in a similar fashion as that described in Example 331, General Procedure XX by dehydration of Compound **669** (Structure **115** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 3, Z = methylene). Compound **670** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 8.86 (br s, 1 H), 7.17 (dd, J = 1.7, 8.2, 1 H), 7.05 (d, J = 1.7, 1 H), 6.77 (d, J = 8.2, 1 H), 6.03 (t, J = 6.7, 1 H), 2.56 (m, 2 H), 2.28 (m, 2 H), 1.85 (m, 2 H), 1.73 (s, 6 H), 1.65 (m, 4 H).

EXAMPLE 370

6-(1-Cycloheptyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **671**, Structure **118** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 3, Z = methylene)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compound **670** (Structure **116** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 3, Z = methylene). Compound **671** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 8.34 (br s, 1 H), 7.05 (d, J = 8.1, 1 H), 6.92 (s, 1 H), 6.73 (d, J = 8.1, 1 H), 2.62 (m, 1 H), 1.85 to 1.51 (m, 24 H).

EXAMPLE 371

6-(2,6,6-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **672**, Structure **116** of Scheme XXIII, where $R^4 = R^7 = R^8$ = methyl, $R^5 = R^6 = H$, n = 2, Z = methylene)

This compound was prepared in a similar fashion as that described in Examples 330 and 331, General Procedures XIX and XX by using Compound **663** (Structure **114** of Scheme XXIII) and 2,2,6-trimethylcyclohexanone. Compound **672** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 9.85 (br s, 1 H), 8.21 (d, J = 8.4, 1 H), 7.30 (d under dd, 2 H), 5.92 (s, 1 H), 2.38 (m, 2 H), 2.18 (s, 3 H), 1.85 (m, 2 H), 1.75 (m, 8 H), 1.33 (s, 3 H).

EXAMPLE 372

(±)-6-(3,3,5-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **673**, Structure **116** of Scheme XXIII, where $R^4 = R^7 = R^8 = H$, $R^5 = R^6 =$ methyl, n = 1, Z = 2-methylethylene) and (±)-6-(3,5,5-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **674**, Structure **116** of Scheme XXIII, where $R^4 = R^5 = R^7 = R^8 = H$, $R^6 =$ methyl, n = 1, Z = 2,2-dimethylethylene)

These compounds were prepared in a similar fashion as that described in Examples 330 and 331, General Procedures XIX and XX by using Compound **663** (Structure **114** of Scheme XXIII) and 3,3,5-trimethylcyclohexanone. Compounds **673** and **674** were isolated as a 1/1 mixture as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.60 (br s, 2 H), 7.24 (dd, J = 2.0, 8.1, 2 H), 7.13 (d, J = 2.0, 2 H), 6.78 (d, J = 8.1, 2 H), 5.85 (s, 1 H), 5.74 (s, 1 H), 2.35 (m, 2 H), 2.20 (m, 2 H), 2.04 (m, 2 H), 1.92 (m., 2 H), 1.74 (s, 6 H), 1.73 (s, 6 H), 1.51 (m, 4 H), 1.08 (m, 18 H).

EXAMPLE 373

(±)-6-(5-Methyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **675**, Structure **116** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 2, Z = methylmethine) and (±)-6-(3-Methyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **676**, Structure **116** of Scheme XXIII, where $R^4 = R^6 = R^7 = R^8 = H$, $R^5 =$ methyl, n = 1, Z = ethylene)

These compounds were prepared in a similar fashion as that described in Examples 330 and 331, General Procedures XIX and XX by using Compound **663** (Structure **114** of Scheme XXIII) and 3-methylcyclohexanone. Compounds **675** and **676** were isolated as a 2/1 mixture as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.62 (br s, 2 H), 7.25 (dd, J = 2.0, 8.2, 2 H), 7.14 (d, J = 2.0, 2 H), 6.77 (d, J = 8.2, 2 H), 6.04 (s, 1 H), 5.89 (s, 1 H), 2.43 to 2.25 (m, 13 H), 1.73 (s, 6 H), 1.72 (s, 6H), 1.07 (m, 6 H).

EXAMPLE 374

(±)-6-(2,6-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **677**, Structure **116** of Scheme XXIII, where R^4 = R^8 = methyl, R^5 = R^6 = R^7 = H, n = 2, Z = methylene)

This compound was prepared in a similar fashion as that described in Examples 330 and 331, General Procedures XIX and XX by using Compound **663** (Structure **114** of Scheme XXIII) and 2,6-dimethylcyclohexanone. Compound **677** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.86 (br s, 1 H), 6.94 (dd, *J* = 1.6, 8.0, 1 H), 6.85 (d, *J* = 1.6, 1 H), 6.73 (d, *J* = 8.0, 1 H), 2.42 (br m, 1 H), 2.05 (m, 2 H), 1.81 (m, 1 H), 1.71 (s, 3 H), 1.70 (s, 3 H), 1.65 (m, 2 H), 1.47 (s, 3 H), 0.79 (d, *J* = 6.9, 3 H).

EXAMPLE 375

(±)-6-(2-Bicyclo[2.2.1]heptenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **678**, Structure **116** of Scheme XXIII, where R^5R^8 = bridged ethylene, R^4 = R^5 = R^8 = H, n = 1, Z = methylene)

This compound was prepared in a similar fashion as that described in Examples 330 and 331, General Procedures XIX and XX by using Compound **663** (Structure **114** of Scheme XXIII) and 2-norbornanone. Compound **678** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.44 (br s, 1 H), 7.28 (d, *J* = 8.3, 1 H), 7.16 (s, 1 H), 6.77 (d, *J* = 8.3, 1 H), 6.22 (d, *J* = 3.0, 1 H), 3.27 (s, 1 H), 3.00 (s, 1 H), 1.83 (m, 2 H), 1.77 (s, 3 H), 1.76 (s, 3 H), 1.52 (m, 1 H), 1.25 (m, 1 H), 1.10 (m, 2 H).

EXAMPLE 376

(±)-6-(4,5-*trans*-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **679**, Structure **116** of Scheme XXIII, where R^4 = R^5 = R^6 = R^7 = R^8 = H, n = 1, Z = 1,2-*trans*-dimethylethylene) and (±)-6-(3,4-*trans*-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **680**, Structure **116** of Scheme XXIII, where R^4 = R^6 = R^7 = R^8 = H, R^5 = methyl, n = 1, Z = 2-methylethylene)

These compounds were prepared in a similar fashion as that described in Examples 330 and 331, General Procedures XIX and XX by using Compound **663** (Structure **114** of Scheme XXIII) and *trans*-3,4-dimethylcyclohexanone. Compounds **679** and **680** were isolated as a 2/1

mixture as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.68 (br s, 2 H), 7.25 (dd, J = 1.8, 8.4, 2 H), 7.14 (d, J = 1.8, 2 H), 6.78 (d, J = 8.4, 2 H), 6.00 (br t, 1 H), 5.83 (s, 1 H), 2.35 to 2.25 (m, 4 H), 2.05 (m, 4 H), 1.85 (m, 4 H), 1.73 (s, 6 H), 1.72 (s, 6H), 1.26 (m, 2 H), 1.03 (m, 12 H).

EXAMPLE 377

6-(6,6-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **681**, Structure **116** of Scheme XXIII, where R^7 = R^8 = methyl, R^4 = R^5 = R^6 = H, n = 2, Z = methylene)

This compound was prepared in a similar fashion as that described in Examples 330 and 331, General Procedures XIX and XX by using Compound **663** (Structure **114** of Scheme XXIII) and 2,2-dimethylcyclohexanone. Compound **681** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.53 (br s, 1H), 6.99 (dd, J = 1.7, 8.0, 1 H), 6.88 (d, J = 1.7, 1 H), 6.73 (d, J = 8.0, 1 H), 5.42 (t, J = 3.7, 1 H), 2.11 (m, 2 H), 1.71 (m, 8 H), 0.99 (s, 6 H).

EXAMPLE 378

6-(5,5-Dimethyl-1-)cyclopentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **682**, Structure **116** of Scheme XXIII, where R^7 = R^8 = methyl, R^4 = R^5 = R^6 = H, n = 1, Z = methylene)

This compound was prepared in a similar fashion as that described in Examples 330 and 331, General Procedures XIX and XX by using Compound **663** (Structure **114** of Scheme XXIII) and 2,2-dimethylcyclopentanone. Compound **511** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.02 (br s, 1 H), 7.19 (dd, J = 1.8, 8.1, 1 H), 7.09 (d, J = 1.8, 1 H), 6.73 (d, J = 8.1, 1 H), 5.70 (t, J = 2.4, 1 H), 2.36 (td, J = 2.5, 7.1, 1 H), 1.86 (t, J = 7.1, 1 H), 1.72 (s, 6 H), 1.18 (s, 6 H).

EXAMPLE 379

(±)-6-(3,3,5-*cis*-Trimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **683**, Structure **118** of Scheme XXIII, where $R^4 = R^7 = R^8 = H$, $R^5 = R^6$ = methyl, n = 1, Z = 2-methylethylene) and (±)-6-(3,3,5-*trans*-Trimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **684**, Structure **118** of Scheme XXIII, where $R^4 = R^7 = R^8 = H$, $R^5 = R^6$ = methyl, n = 1, Z = 2-methylethylene)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compounds **673/674** (Structure **116** of Scheme XXIII, where $R^4 = R^7 = R^8 = H$, $R^5 = R^6$ = methyl, n = 1, Z = 2-methylethylene). Compounds **683** and **684** were isolated as a 2/1 mixture as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 8.39 (br s, 2 H), 7.15 (dd, *J* = 1.7, 8.2, 1 H), 7.07 (dd, *J* = 1.7, 8.2, 1 H), 6.97 (d, *J* = 1.7, 1 H), 6.92 (d, *J* = 1.7, 1 H), 6.75 (d, *J* = 8.2, 2 H), 2.90 (m, 1 H), 2.70 (m, 1 H), 2.05 (m, 1 H), 1.72 (s, 12 H).

EXAMPLE 380

(±)-6-(3-*cis*-Methyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **685**, Structure **118** of Scheme XXIII, where $R^4 = R^6 = R^7 = R^8 = H$, R^5 = methyl, n = 1, Z = ethylene) and (±)-6-(3-*trans*-Methyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **686**, Structure **118** of Scheme XXIII, where $R^4 = R^6 = R^7 = R^8 = H$, R^5 = methyl, n = 1, Z = ethylene)

These compounds were prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of compounds **675/676** (Structure **116** of Scheme XXIII, where $R^4 = R^6 = R^7 = R^8 = H$, R^5 = methyl, n = 1, Z = ethylene). Compounds **685** and **686** were isolated as a 2/1 mixture as a white solid: (major isomer) ^1H NMR (400 MHz, $CDCl_3$) 7.86 (bs, 1 H), 7.08 (dd, *J* = 8.4, 2.1, 1 H), 6.95 (d, *J* = 2.1, 1 H), 6.75 (d, *J* = 8.4, 1 H), 2.59 (m, 1 H), 2.05 (m, 1 H), 1.88-1.28 (m, 8 H), 1.72 (s, 6 H), 0.94 (d, *J* = 7.5, 3 H); (minor isomer) ^1H NMR (400 MHz, $CDCl_3$) 7.86 (bs, 1 H), 7.10 (dd, *J* = 8.4, 2.1, 1 H), 6.97 (d, *J* = 2.1, 1 H), 6.75 (d, *J* = 8.4, 1 H), 2.79 (m, 1 H), 2.05 (m, 1 H), 1.88-1.28 (m, 8 H), 1.72 (s, 6 H), 1.08 (d, *J* = 7.5, 3 H).

EXAMPLE 381

(±)-6-(2,6-cis,cis-Dimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound 687, Structure 118 of Scheme XXIII, where $R^5 = R^6 = R^7 = H$, $R^4 = R^8$ = methyl, n = 1, Z = ethylene)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compound **677** (Structure **116** of Scheme XXIII, where $R^4 = R^8$ = methyl, $R^5 = R^6 = R^7 = H$, n = 2, Z = methylene). Compound **687** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 7.36 (br s, 1 H), 7.17 (d, J = 8.2, 1 H), 7.02 (s, 1 H), 6.65 (d, J = 8.2, 1 H), 2.74 (m, 1 H), 1.86 (m, 2 H), 1.71 (s, 6 H), 1.50 to 1.40 (m, 4 H), 0.63 (d, J = 7.1, 6 H).

EXAMPLE 382

(*E*)-6-(1,4-Dimethyl-1-)pentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound 688, Structure 116 of Scheme XXIII, where R^4 = methyl, R^6 = isopropyl, $R^5 = R^7 = R^8 = H$, n = 1, Z = two no-bond hydrogens)

This compound was prepared in a similar fashion as that described in Examples 330 and 331, General Procedures XIX and XX by using Compound **663** (Structure **114** of Scheme XXIII) and 5-methyl-2-hexanone. Compound **688** was isolated as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) 8.92 (br s, 1 H), 7.23 (dd, J = 1.7, 8.0, 1 H), 7.11 (d, J = 1.7, 1 H), 6.79 (d, J = 8.0, 1 H), 5.73 (t, J = 8.0, 1 H), 2.07 (t, J = 8.0, 2 H), 1.94 (s, 3 H), 1.71-1.73 (m, 3 H), 1.72 (s, 6 H), 0.96 (s, 3 H), 0.94 (s, 3 H).

EXAMPLE 383

6-(1-Cyclohexenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound 689, Structure 117 of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 2, Z = methylene)

This compound was prepared in a similar method as that described in Example 95, General Procedure XI by treatment of Compound **667** (Structure **116** of Scheme XXIII, where $R^4 = R^5 = R^6 = R^7 = R^8 = H$, n = 2, Z = methylene) with Lawesson's reagent. Compound **689** was isolated as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 9.60 (br s, 1 H), 7.29 (dd, J = 1.8, 8.2, 1 H), 7.13 (d, J = 1.8, 1 H), 6.81(d, J = 8.2, 1 H), 6.08 (t, J = 4.0, 1 H), 2.35 (m, 2 H), 2.20 (m, 2 H), 1.80 to 1.76 (m, 8 H), 1.68 to 1.60 (m, 2 H).

EXAMPLE 384

6-(3-Oxo-1-)cyclopentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound 690, Structure 119 of Scheme XXIV, where Y = O, n = 0)

Compound **690** was made according to Examples 330 and 331, General Procedures XIX and XX by using Compound **663** (Structure **114** of Scheme XXIV) and 3-ethoxy-2-cyclopenten-1-one as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.53 (br s, 1 H), 7.56 (dd, J = 1.8, 8.3, 1 H), 7.42 (d, J = 1.8, 1 H), 6.91 (d, J = 8.3, 1 H), 6.52 (s, 1 H), 3.02 (m, 2 H), 2.60 (m, 2 H), 1.75 (s, 6 H).

EXAMPLE 385

6-(3-Oxo-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound 691, Structure 119 of Scheme XXIV, where Y = O, n = 1)

Compound **691** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **663** (Structure **114** of Scheme XXIV) and 3-ethoxy-2-cyclohexen-1-one as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.05 (br s, 1 H), 7.44 (dd, J = 1.9, 8.3, 1 H), 7.34 (d, J = 1.9, 1 H), 6.85 (d, J = 8.3, 1 H), 6.34 (s, 1 H), 2.75 (t, J = 5.4, 2 H), 2.49 (t, J = 5.4, 2 H), 2.16 (quintet, J = 5.4, 2 H), 1.75 (s, 6 H).

EXAMPLE 386

(±)-6-(3-Hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound 692, Structure 120 of Scheme XXIV, where Y = O, n = 1)

This compound was prepared in a similar fashion as that described in Example 358, General Procedure XXI by reduction of Compound **691** (Structure **119** of Scheme XXIV, where Y = O, n = 1). Compound **692** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.70 (br s,1 H), 7.27 (d, J = 8.2, 1 H), 7.18 (s, 1 H), 6.80 (d, J = 8.2, 1 H), 6.08 (s, 1 H), 4.40 (br s, 1 H), 2.41 to 2.36 (m, 2 H), 1.94 to 1.92 (m, 2 H), 1.71 (s, 6 H), 1.70 to 1.63 (m, 3 H).

EXAMPLE 387

(±)-6-(3-*cis*-Hydroxy)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound 693, Structure 121 of Scheme XXIV, where n = 1)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compound **692** (Structure **120** of Scheme XXIV, where Y =

O, n = 1). Compound **693** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.70 (br s, 1 H), 7.27 (d, J = 8.2, 1 H), 7.18 (s, 1 H), 6.80 (d, J = 8.2, 1 H), 6.08 (s, 1 H), 4.40 (br s, 1 H), 2.41 to 2.36 (m, 2 H), 1.94 to 1.92 (m, 2 H), 1.71 (s, 6 H), 1.70 to 1.63 (m, 3 H).

EXAMPLE 388

(±)-6-(3'-Butyl-3-hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **694**, Structure **122** of Scheme XXIV, where n = 1)

To a solution of Compound **691** (Structure **119** of Scheme XXIV, where Y = O, n = 1)_15 mg, 0.06 mmol) in dry THF (4 mL) at –78 °C, was added a 1.6 M n-BuLi solution in hexane (0.04 mL). After 1 h the reaction was quenched with saturated NH_4Cl and extracted with EtOAc (10 mL). The organic layer was washed with brine (3 x 5 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by PTLC (20 x 20 cm, 250 µm, 30% EtOAc/hex) to afford 10 mg (56%) of Compound **694** as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) 8.90 (br s, 1 H), 7.26 (dd, J = 1.7, 8.2, 1 H), 7.15 (d, J = 1.7, 1 H), 6.81 (d, J = 8.2, 1 H), 5.91 (s, 1 H), 2.38 (m, 2 H), 1.86 (m, 2 H), 1.80 to 1.61 (m, 10 H), 1.39 (m, 4 H), 0.93 (t, J = 7.1, 3 H).

EXAMPLE 389

6-(3-Oxo-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **695**, Structure **119** of Scheme XXIV, where Y = S, n = 1)

6-Bromo-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **696**, Structure **118a** of Scheme XXIV):

This compound was prepared in a similar fashion as that described in Example 95, General Procedure XI from Compound **663** (Structure **114** of Scheme XXIV) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 10.08 (br s, 1 H), 7.41 (dd, J = 2.0, 8.4, 1 H), 7.27 (d, J = 2.0, 1 H), 6.81 (d, J = 8.4, 1 H), 1.73 (s, 6 H).

6-(3-Oxo-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **695**, Structure **119** of Scheme XXIV, where Y = S, n = 1):

Compound **695** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **696** and 3-ethoxy-2-cyclohexen-1-one as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) 9.80 (br s, 1 H), 7.50 (dd, J = 1.7, 8.3, 1 H), 7.34 (d, J = 1.7, 1 H), 6.95 (d, J = 8.3, 1 H), 6.42 (s, 1 H), 2.75 (t, J = 6.3, 2 H), 2.51 (t, J = 6.3, 2 H), 2.17 (m, 2 H), 1.78 (s, 6 H).

EXAMPLE 390

(±)-6-(3-Hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **697**, Structure **120** of Scheme XXIV, where Y = S, n = 1)

This compound was prepared in a similar fashion as that described in Example 358, General Procedure XXI by reduction of Compound **695** (Structure **119** of Scheme XXIV, where Y = S, n = 1). Compound **697** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.90 (br s, 1 H), 7.31 (dd, J = 1.6, 8.1, 1 H), 7.19 (d, J = 1.6, 1 H), 6.75 (d, J = 8.1, 1 H), 6.09 (s, 1 H), 4.42 (br m, 1 H), 2.35 (m, 1 H), 1.95 (m, 2 H), 1.75 (s, 6 H), 1.74 (m, 2 H).

EXAMPLE 391

(±)-6-(1-Cyclohexenyl)-1,4-dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **698**, Structure **127** of Scheme XXV, where $R^1 = R^3$ = H, R^2 = methyl, W = O)

(±)-1,4-Dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **699**, Structure **125** of Scheme XXV, where $R^1 = R^3$ = H, R^2 = methyl, W = O):

To a solution of 2-*tert*-butoxycarbonylamino-α-methylbenzyl alcohol (0.58 g, 2.4 mmol) and 1,2-dichloroethane (10 mL) was added TsOH (0. 5g, 2.6 mmol) and the reaction mixture was heated to reflux. After 20 minutes the reaction was quenched with saturated $NaHCO_3$ (10 mL) and extracted with EtOAc (20 mL). The organic layer was washed with brine (3x 5 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by flash chromatography (50% EtOAc/hex) to afford 0.30 g (75%) of Compound **699** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.64 (br s, 1 H), 7.27 (t, J = 7.8, 1 H), 7.08 (d overlapping t, 2 H), 6.86 (d, J = 7.8, 1 H), 5.50 (q, J = 6.7, 1 H), 1.71 (d, J = 6.7, 3 H).

(±)-6-Bromo-1,4-dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **700**, Structure **126** of Scheme XXV, where $R^1 = R^3$ = H, R^2 = methyl, W = O):

To a solution of Compound **699** (0.15 g, 0.64 mmol) in CCl_4 (15 mL) was added bromine (0.1 mL, 0.64 mmol). Stirred at room temperature for 1 hr. The reaction mixture was concentrated in vacuo to afford an orange solid. Washed solid with hot hexane and filtered to afford 130 mg (84%) of Compound **700** as a tan solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.74 (br s, 1 H), 7.37 (dd, J = 1.7, 8.5, 1 H), 7.25 (d under solvent peak, 1 H), 6.70 (d, J = 8.5 ; 1 H), 5.45 (q, J = 6.6, 1 H), 1.70 (d, J = 6.6, 1 H).

(±)-6-(1-Cyclohexenyl)-1,4-dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **698**, Structure **127** of Scheme XXV, where $R^1 = R^3 = H$, R^2 = methyl, W = O):

Compound **527** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **700** and cyclohexanone as a white solid: ^1H NMR (400 MHz, $CDCl_3$) 8.60 (br s, 1 H), 7.26 (dd under solvent peak, 1 H), 7.09 (d, J = 1.7, 1 H), 6.78 (d, J = 8.2, 1 H), 6.07 (m, 1 H), 5.50 (q, J = 6.7, 1 H), 2.38 (m, 2 H), 2.19 (m, 1 H), 1.78 (m, 2 H), 1.71 (d, J = 6.7, 3 H), 1.67 (m, 2 H).

EXAMPLE 392

6-(1-Cyclohexenyl)-1,4-dihydro-4,4,5-trimethyl-1,3-benzo[d]oxazin-2-one (Compound 701, Structure 127 of Scheme XXV, where $R^1 = R^2 = R^3$ = methyl, W = O)

2-(1-Hydroxyisopropyl)-3-methylaniline (Compound **702**, Structure **124** of Scheme XXV, where $R^1 = R^2 = R^3$ = methyl):

To a solution of 2-amino-6-methylbenzoic acid (Structure **123** of Scheme XXV, where R^3 = methyl) (0.50 g, 3.3 mmol) and dry THF (20 mL) was added 3 M MeMgCl in THF (11 mL) at 0 °C. The reaction was heated to 50 °C and stirred for 15 hrs. The reaction mixture was cooled to room temperature then poured into saturated NH_4Cl (20 mL) and extracted with EtOAc (20 mL). The organic layer was washed with brine (3 x 5 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by flash chromatography (100% hexane to 50% EtOAc/hex gradient) to afford 0.36 g (65%) of Compound **702** as a light orange oil: ^1H NMR (400 MHz, $CDCl_3$) 6.89 (t, J = 7.7, 1 H), 6.52 (d under d, J = 7.7, 2 H), 2.40 (s, 3 H), 1.75 (s, 6 H).

1,4-Dihydro-4,4,5-trimethyl-1,3-benzo[d]oxazin-2-one (Compound **703**, Structure **125** of Scheme XXV, where $R^1 = R^2 = R^3$ = methyl, W = O):

To a solution of Compound **702** (0.36 g, 2.2 mmol) and dry THF (10 mL) was added DMAP (0.29 g, 2.4 mmol) and 1,1'-carbonyldiimidazole (0.39 g, 2.4 mmol). The reaction mixture was heated to 50 °C for 1.5 hrs. The reaction mixture was cooled to room temperature then poured into saturated NH_4Cl (20 mL) and extracted with EtOAc (20 mL). The organic layer was washed with brine (3 x 5 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The crude product was purified by flash chromatography (50% EtOAc/hex) to afford 0.40 g (95%) of

Compound **703** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.97 (br s, 1 H), 7.10 (t, J = 7.8, 1 H), 6.85 (d, J = 7.8, 1 H), 6.64 (d, J = 7.8, 1 H), 2.41 (s, 3 H), 1.80 (s, 6 H).

6-Bromo-1,4-dihydro-4,4,5-trimethyl-1,3-benzo[d]oxazin-2-one (Compound **704**, Structure **126** of Scheme XXV, where $R^1 = R^2 = R^3$ = methyl, W = O):

To a solution of Compound **703** (100 mg, 0.52 mmol) and CCl_4 (5 mL) was added bromine (0.05 mL, 1.0 mmol). Stirred at room temperature for 1.0 hr. The reaction mixture was concentrated in vacuo to afford an orange solid. Washed solid with hot hexane and filtered to afford 140 mg (100%) of Compound **704** as a tan solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.18 (br s, 1 H), 7.44 (d, J = 8.5, 1 H), 6.54 (d, J = 8.5, 1 H), 2.49 (s, 3 H), 1.83 (s, 6 H).

6-(1-Cyclohexenyl)-1,4-dihydro-4,4,5-trimethyl-1,3-benzo[d]oxazin-2-one (Compound **701**, Structure **127** of Scheme XXV, where $R^1 = R^2 = R^3$ = methyl, W = O):

Compound **701** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **704** and cyclohexanone as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.52 (br s, 1 H), 6.94 (d, J = 8.0, 1 H), 6.55 (d, J = 8.0, 1 H), 5.52 (m, 1 H), 2.29 (s, 3 H), 2.16 to 2.11 (m, 4 H), 1.18 (s, 6 H), 1.75 to 1.67 (m, 4 H).

EXAMPLE 393

6-(1-Cyclohexenyl)-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound 705, Structure 127 of Scheme XXV, where $R^1 = R^2$ = methyl, R^3 = H, W = methylene)

6-Bromo-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **706**, Structure **126** of Scheme XXV, where $R^1 = R^2$ = methyl, R^3 = H, W = methylene):

To a solution of Compound **504** (Structure **125** of Scheme XXV, where $R^1 = R^2$ = methyl, R^3 = H, W = methylene) (0.20 g, 1.1 mmol) and CCl_4 (20 mL) was added bromine (0.05 mL, 1.1 mmol). Stirred at room temperature for 1.5 hrs. The reaction mixture was concentrated in vacuo to afford an orange solid. Washed solid with hot hexane and filtered to afford 0.20 g of Compound **706** in 67% yield as a light orange solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.40 (br s, 1 H), 7.41 (d, J = 2.1, 1 H), 7.31 (dd, J = 2.1, 8.4, 1 H), 6.72 (d, J = 8.4, 1 H), 2.50 (s, 2 H), 1.33 (s, 6 H).

6-(1-Cyclohexenyl)-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **705**, Structure **127** of Scheme XXV, where $R^1 = R^2$ = methyl, R^3 = H, W = methylene):

Compound **705** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **706** and cyclohexanone as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.05 (br s, 1 H), 7.31 (d, J = 1.8, 1 H), 7.18 (dd, J = 1.8, 8.3, 1 H), 6.71 (d, J = 8.3, 1 H), 6.07 (td, J = 2.3, J = 4.1, 1 H), 2.48 (s, 2 H), 2.39 (m, 2 H), 2.20 (m, 2 H), 1.78 (m, 2 H), 1.66 (m, 2 H), 1.34 (s, 6 H).

EXAMPLE 394

6-Cyclohexyl-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **707**, Structure **128** of Scheme XXV)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compound **705** (Structure **127** of Scheme XXV, where R^1 = R^2 = methyl, R^3 = H, W = methylene). Compound **707** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.03 (br s, 1 H), 7.11 (d, J = 1.5, 1 H), 7.01 (dd, J = 1.5, J = 8.0, 1 H), 6.69 (d, J = 8.0, 1 H), 2.47 (s, 2 H), 1.87 to 1.74 (m, 4 H), 1.42 to 1.26 (m, 13 H).

EXAMPLE 395

(±)-8-Bromo-6-(1-cyclohexenyl)-1,4-dihydro-4-trifluoromethyl-1,3-benzo[d]oxazin-2-one (Compound **708**, Structure **132** of Scheme XXVI)

(±)-N-*tert*-Butoxycarbonyl-2-(1-hydroxy-2,2,2-trifluoroethyl)aniline (Compound **709**, Structure **129** of Scheme XXVI):

To a solution of N-*tert*-Boc-2-bromoaniline (1.0 mL, 3.8 mmol) in dry Et_2O/THF (1:1, 10 mL) was added 1.4 M MeLi/Et_2O (3.3 mL) at room temperature. After 15 min. the white turbid mixture was cannulated into a flask charged with 1.7 M t-BuLi/pentane (5 mL) and dry Et_2O/THF (1:1, 10 mL) at –78 °C. Stirred at –78 °C for 1 hr then added ethyltrifluoroacetate (2.5 mL, 21 mmol, freshly distilled). Allowed reaction to slowly warm to rt overnight. Quenched with saturated NH_4Cl and extracted with EtOAc. Washed organic layer with brine, dried (Na_2SO_4) and concentrated in vacuo to afford a yellow oil. Purified by flash chromatography (hex to 25% EtOAc/hex) to give the desired 2-N-Boc-aminotriflouroacetophenone (0.28 g) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.13 (d, J = 7.4, 1 H), 7.38 (dd, J = 1.5, 7.4, 1 H), 7.28 (t, J = 7.4, 1 H), 6.99 (brs, 1 H), 6.91 (dt, J = 1.5, 7.4, 1 H), 1.52 (m, 9 H). The trifluoroacetophenone was treated with $NaBH_4$ in methanol followed by standard work-up to

afford Compound **709** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.76 (d, *J* = 7.9, 1 H), 7.38 (m, 2 H), 7.14 (t, *J* = 7.9, 1 H), 5.15 (m, 1 H), 3.34 (d, *J* = 4.4, 1 H), 1.51 (m, 9 H).

(±)-1,4-Dihydro-4-trifluoromethyl-1,3-benzo[d]oxazin-2-one (Compound **710**, Structure **130** of Scheme XXVI):

To a solution of Compound **709** (0.24 g, 0.82 mmol) in dichloromethane (15 mL) was added TsOH (160 mg). Heated to reflux for 1.5 hr. Quenched with saturated $NaHCO_3$. Extracted with EtOAc, washed organic layer with brine, dried (Na2SO4) and concentrated in vacuo to afford 150 mg of Compound **710** as a white solid (84%): ^{1}H NMR (400 MHz, $CDCl_3$) 7.23 (m, 2 H), 6.87 (t, *J* = 7.7, 1 H), 6.78 (d, *J* = 7.7, 1 H), 5.07 (q, *J* = 7.4, 1 H).

(±)-6,8-Dibromo-1,4-dihydro-4-trifluoromethyl-1,3-benzo[d]oxazin-2-one (Compound **711**, Structure **131** of Scheme XXVI):

To a solution of Compound **710** (50 mg, 0.23 mmol) and CCl_4 (5 mL) was added bromine (0.01 mL, 0.23 mmol) at room temperature. After 1 hr the reaction was concentrated *in vacuo* to afford a yellow foamy solid. Washed solid with hexane to afford 35 mg (41%) of Compound **711** as a solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.35 (s, 1 H), 7.29 (dd, *J* = 2.4, 8.5, 1 H), 6.64 (d, *J* = 8.5, 1 H), 5.04 (q, *J* = 7.0, 1 H), 4.00 (brs, 1 H).

(±)-8-Bromo-6-(1-cyclohexenyl)-1,4-dihydro-4-trifluoromethyl-1,3-benzo[d]oxazin-2-one (Compound **708**, Structure **132** of Scheme XXVI):

Compound **537** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **711** and cyclohexanone as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.52 (d, *J* = 2.0, 1 H), 7.19 (d, *J* = 2.0, 1 H), 6.01 (m, 1 H), 5.08 (m, 1 H), 4.50 (brs, 1 H), 2.31 (m, 2 H), 2.17 (m, 2 H), 1.76 (m, 2 H), 1.64 (m, 2 H).

EXAMPLE 396

5-(3-Oxo-1-)cyclohexenyl-3,3-dimethyl-2-indolone (Compound 712, Structure 134 of Scheme XXVII, where $R^1 = R^2$ = methyl, R^3R^4 = carbonyl, n = 2)

5-Bromo-3,3-dimethyl-2-indolone (Compound **713**, Structure **133** of Scheme XXVII, where $R^1 = R^2$ = methyl):

This compound was prepared by the following General Procedure XXII (Alkylation and bromination of 2-indolone):

To a solution of 2-indolone (200 mg, 1.5 mmol) in dry THF (15 mL) and TMEDA (0.45 mL, 3.0 mmol) at –78 °C was added *n*-BuLi (1.9 mL, 1.6M in hex.). The reaction mixture was warmed to –20 °C and iodomethane was added (0.1 mL, 1.5 mmol). After 1 hr, added another equivalent of iodomethane (0.1 mL, 1.5 mmol). Warmed reaction mixture to room temperature and stirred for 15 hrs. Quenched reaction with saturated NH_4Cl (10 mL) and extracted with EtOAc (20 mL). The organic layer was washed with brine (3 x 10 mL), dried (Na_2SO_4), and concentrated *in vacuo*. Purified by flash chromatography (10% hexane/EtOAc to 50% hexane/EtOAc gradient) to afford 126 mg (52%) of 3,3-dimethyl-2-indolone as a white solid. Next, to a solution of the 3,3-dimethyl-2-indolone (126 mg, 0.78 mmol) and CCl4 (10 mL) was added bromine (0.04 mL, 0.78 mmol) at room temperature. After 1 hr, the reaction mixture was partitioned between EtOAc (10 mL) and brine (5 mL). The organic layer was washed with brine (3 x 5 mL), dried (Na_2SO_4), and concentrated *in vacuo* to afford 180 mg (96%) of Compound **713** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 9.00 (br s, 1 H), 7.38 (d, *J* = 8.2, 1 H), 7.35 (s, 1 H), 6.97 (d, *J* = 8.2, 1 H), 1.44 (s, 6 H).

5-(3-Oxo-1-)cyclohexenyl-3,3-dimethyl-2-indolone (Compound **712**, Structure **134** of Scheme XXVII, where $R^1 = R^2$ = methyl, R^3R^4 = carbonyl, n = 2):

Compound **712** was made according to General Procedures XIX and XX in Examples 330 and 331 from Compound **713** and 3-ethoxy-2-cyclohexen-1-one as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 9.45 (br s, 1 H), 7.45 (d under dd, 2 H), 7.02 (d, *J* = 8.0, 1 H), 6.44 (s, 1 H), 2.79 (t, *J* = 6.1, 2 H), 2.50 (t, *J* = 6.1, 2 H), 2.17 (m, 2 H), 1.44 (s, 6 H).

EXAMPLE 397

(±)-5-(3-Hydroxy-1-)cyclohexenyl-3,3-dimethyl-2-indolone (Compound 714, Structure 135 of Scheme XXVII, n = 2)

This compound was prepared in a similar fashion as that described in Example 358, General Procedure XXI by reduction of Compound **712** (Structure **134** of Scheme XXVII, where $R^1 = R^2$ = methyl, R^3R^4 = carbonyl, n = 2). Compound **714** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.96 (br s, 1 H), 7.24 (d under dd, 2 H), 6.09 (br d, 1 H), 4.41 (br s, 1 H), 2.39 (m, 2 H), 1.93 (m, 2 H), 1.76 to 1.58 (m, 3 H), 1.40 (s, 6 H).

EXAMPLE 398

(±)-5-(3-Oxocyclohexyl)-3,3-dimethyl-2-indolone (Compound 715, Structure 136 of Scheme XXVII, where $R^1 = R^2$ = methyl, R^3R^4 = carbonyl, n = 2)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure III by hydrogenation of Compound **712** (Structure **134** of Scheme XXVII, where $R^1 = R^2$ = methyl, R^3R^4 = carbonyl, n = 2). Compound **715** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.03 (d under dd, 2 H), 6.78 (d, J = 8.5, 1 H), 2.49 (m, 1 H), 1.86 (m, 3H), 1.81 (m, 1 H), 1.39 to 1.25 (m, 10 H).

EXAMPLE 399

5-Cyclohexyl-3,3-spirocyclohexyl-2-indolone (Compound 716, Structure 136 of Scheme XXVII, where R^1R^2 = spirocyclohexyl, $R^3 = R^4$ = H, n = 2)

5-Bromo-3,3-spirocyclohexyl-2-indolone (Compound **717**, Structure **133** of Scheme XXVII, where R^1R^2 = spirocyclohexyl):

This compound was prepared in a similar fashion as that described in Example 396, General Procedure XXII but using 1,5-diiodopentane in place of iodomethane. Compound **717** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.98 (bs, 1H), 7.54 (s, 1H), 7.33 (dd, J = 1.2, 8.2, 1H), 6.78 (d, 8.2, 1H), 1.94-1.58 (m, 10H).

5-Cyclohexyl-3,3-spirocyclohexyl-2-indolone (Compound **716**, Structure **136** of Scheme XXVII, where R^1R^2 = spirocyclohexyl, $R^3 = R^4$ = H, n = 2):

Compound **716** was made according to General Procedures XIX, XX and III in Examples 330, 331 and 1 from Compound **717** and cyclohexanone as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.97 (bs, 1H), 7.27 (s, 1H), 7.04 (dd, J = 1.1, 7.8, 1H), 6.81 (d, J = 7.9, 1H), 2.48 (m, 1H), 1.94-1.65 (mm, 18H), 1.43-1.37 (m, 4H).

EXAMPLE 400

5-Cyclopentyl-3,3-spirocyclohexyl-2-indolone (Compound 718, Structure 136 of Scheme XXVII, where R^1R^2 = spirocyclohexyl, $R^3 = R^4$ = H, n = 1)

Compound **718** was made according to General Procedures XIX, XX and III in Examples 330, 331 and 1 from Compound **717** (Structure **133** of Scheme XXVII, where R^1R^2 = spirocyclohexyl) and cyclopentanone as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 8.42 (bs,

1H), 7.31 (s, 1H), 7.08 (dd, J = 1.0, 8.1, 1H), 6.83 (d, J = 8.0, 1H), 2.97 (quint., J = 7.5, 1H), 2.06 (m, 2H), 1.94 (m, 2H), 1.89-1.63 (m, 14H).

EXAMPLE 401

6-(1-Hydroxycyclohexyl)-2(3*H*)-benzothiozolone (Compound **719**, Structure **138** of Scheme XXVIII)

Compound **719** was made according to General Procedures XIX in Examples 330 from 6-bromo-2(3*H*)-benzothiozolone (Structure **137** of Scheme XXVIII) (120 mg, 0.52 mmol) and cyclohexanone (0.11 mL, 1.04 mmol) in 87% yield (113 mg) as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 11.77 (bs, 1 H), 7.63 (d, J = 1.5, 1 H), 7.38 (dd, J = 8.4, 1.5, 1 H), 7.03 (d, J = 8.4, 1 H), 4.70 (s, 1 H), 1.64 (m, 8 H), 1.48 (m, 2 H).

EXAMPLE 402

6-Cyclohexenyl-2(3*H*)-benzothiozolone (Compound **720**, Structure **139** of Scheme XXVIII)

Compound **720** was made according to General Procedures XX in Examples 331 by dehydration of Compound **719** (Structure **138** of Scheme XXVIII) as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 9.38 (s, 1 H), 7.40 (d, J = 1.5, 1 H, 7.29 (dd, J = 8.4, 1.8, 1 H), 7.05 (d, J = 8.4, 1 H), 6.07 (bt, J = 4.0, 1 H), 2.39-2.36 (m, 2 H), 2.21-2.18 (m, 2 H), 1.81-1.75 (m, 2 H), 1.68-1.63 (m, 2 H).

EXAMPLE 403

3,4-Dihydro-6-isopropyl-3-methyl-2(1*H*)-quinazolinone (Compound **721**, Structure **143** of Scheme XXIX, where R = H, $R^1 = R^2$ = methyl)

6-Bromo-3,4-dihydro-3-methyl-2(1*H*)-quinazolinone (Compound **722**, Structure **141** of Scheme XXIX):

In a 100-mL r.b. flask, a solution of commercially available 3,4-dihydro-3-methyl-2(1*H*)-quinazolinone (Structure **140** of Scheme XXIX) (1.0 g, 6.2 mmol) in CH_2Cl_2 (30 mL) was treated with NBS (1.2 g, 6.8 mmol, 1.1 equiv) in portions. The reaction mixture was then allowed to stir at room temperature for 2 h, diluted with CH_2Cl_2 (125 mL), washed with water (2 x 30 mL), Brine (30 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield 1.5 g (99%) of Compound **722** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.26 (m, 1 H), 7.16 (s, 1 H), 6.57 (d, J = 8.4, 1 H), 4.41 (s, 2 H), 3.02 (s, 3 H).

3,4-Dihydro-6-isopropyl-3-methyl-2(1*H*)-quinazolinone (Compound **721**, Structure **143** of Scheme XXIX, where R = H, $R^1 = R^2$ = methyl):

In a 25-mL r.b. flask, dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (4 mg, 0.01-0.02 equiv) was flame-dried under a stream of N_2. The flask was them cooled to –70 °C where a solution of isopropyl magnesium chloride (2 M in THF) (0.62 mL, 3.0 equiv) was added followed by the addition of Compound **551** (100 mg, 0.41 mmol) in THF (2 mL). The reaction mixture was then allowed to warm to room temperature, stirred overnight, quenched with HCl (1 M, 5 mL), diluted with water (5 mL), and extracted with EtOAc (3 x 30 mL). The combined organic layers were then washed with water (15 mL), Brine (20 mL), dried ($MgSO_4$), filtered, and concentrated to give crude product. Compound **721** (5 mg, 6%) was isolated by reverse phase HPLC (ODS, 70% MeOH/water, 2.5 mL/min). Data for Compound **721**: ^{1}H NMR (400 MHz, $CDCl_3$) 7.01 (d, J = 8.3, 1 H), 6.89 (s, 1 H), 6.74 (bs, 1 H), 6.58 (d, J = 8.1, 1 H), 4.43 (s, 2 H), 3.02 (s, 3 H), 2.83 (m, 1 H), 1.21 (d, J = 6.9, 6 H).

EXAMPLE 404

1-Benzyl-6-bromo-3,4-dihydro-3-methyl-2(1*H*)-quinazolinone (Compound 723, Structure 142 of Scheme XXIX)

This compound was prepared in a similar fashion as that described in Example 92, General Procedure X from Compound **722** (Structure **141** of Scheme XXIX) and benzyl bromide. Compound **723** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.29 (m, 2H), 7.21 (m, 3H), 7.17 (m, 2H), 6.55 (d, J = 9.2, 1H), 5.09 (s, 2H), 4.42 (s, 2H), 3.08 (s, 3H).

EXAMPLE 405

1-Benzyl-6-cyclohexyl-3,4-dihydro-3-methyl-2(1*H*)-quinazolinone (Compound 724, Structure 143 of Scheme XXIX, R^1R^2 = cyclohexyl, R = benzyl)

Compound **724** was made according to General Procedures XIX, XX and III in Examples 330, 331 and 1 from Compound **723** (Structure **142** of Scheme XXIX) and cyclohexanone as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.26 (mm, 5H), 6.92 (d, J = 8.5, 1H), 6.88 (s, 1H), 6.62 (d, J = 8.4, 1H), 5.10 (s, 2H), 4.44 (s, 2H), 3.09 (s, 3H), 2.37 (m, 1H), 1.80 (m, 4H), 1.74-1.66 (m, 2H), 1.37-1.27 (m, 4H).

EXAMPLE 406

6-(2,3-Difluoro)phenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 725, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 2,3-difluorine)

2,3-Difluoro-benzeneboronic acid (Compound **726**, Structure **144** of Scheme XXX, where R^2 = 2,3-difluoro):

General Procedure XXIII (Boronic acid formation):

To a solution of an aryl bromide (0.5-1.0 M THF) cooled to –70 °C under an N_2 atmosphere was added *n*-BuLi (1.1 equiv) via syringe pump. The rate of addition is adjusted so that the internal temperature did not rise above –65 °C. After complete addition of *n*-BuLi the reaction mixture was allowed to stir at –70 °C for 3 h before quenching with dry trimethyl borate (3.0 equiv), again adjusting the rate so that the internal temperature did not rise above –65 °C. After complete addition of trimethyl borate the reaction mixture was then slowly warmed to room temperature overnight. The thick reaction mixture was then acidified to pH 2 with an HCl solution, extracted with EtOAc (20 mL/mmol), washed with brine (2 mL/mmol), dried ($MgSO_4$), filtered and concentrated. The crude product was then triturated with hexanes to give the desired boronic acid in quantitative yield.

Compound **726** was prepared according to General Procedure XXIII from 1,2-difluorobenzene (20 g, 0.18 mmol), *n*-BuLi (8.2 M in hexane, 21.4 mL, 0.18 mmol), and trimethyl borate (60 mL, 0.53 mmol) in quantitative yield. Compound **726** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 7.56 (m, 1 H), 7.28 (m, 1 H), 7.15 (mm, 1 H), 5.05 (d, *J* = 5.6, 2 H).

6-(2,3-Difluoro)phenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **725**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 2,3-difluorine):

General Procedure XXIV (Suzuki coupling of 6-bromoquinolinones to aryl boronic acids):

To a 10-mL flask charged with a solution of a 6-bromo-2(1*H*)-quinolinone (25 mg, 0.09 mmol, 1 equiv) in DME (0.1 M) was sequentially added tetrakis(triphenylphosphine)-palladium (0.02-0.05 equiv), aryl boronic acid ($R^2B(OH)_2$) (1.5 equiv, 0.1 M in ethanol), and K_2CO_3 (2.0 equiv, 2.0 M). The yellow reaction mixture was heated to reflux overnight. The now clear reaction solution was cooled, diluted with EtOAc, washed with water (2 x 15 mL), Brine (20

mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The crude product was then purified by trituration with EtOAc/hexane (15%) followed by recrystallization from MeOH/EtOAc to yield the desired product as a white solid in 40-80% overall yield.

Compound **725** was made according to General Procedure XXIV from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and Compound **726** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 12.46 (bs, 1 H), 8.00 (s, 1 H), 7.81 (d, J = 8.6, 1 H), 7.57 (d, J = 8.6, 1 H), 7.21 (m, 3 H), 7.16 (s, 1 H).

EXAMPLE 407

4-Trifluoromethyl-6-(3-nitro)phenyl-2(1*H*)-quinolinone (Compound **727**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3-nitro)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 3-nitrobenzeneboronic acid. Compound **727** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 12.02 (bs, 1 H), 8.45 (d, J = 2.0, 1 H), 8.26 (dd, J = 8.0, 2.3, 1 H), 8.04 (s, 1 H), 7.93 (d, J = 7.7, 1 H), 7.88 (d, J = 8.3, 1 H), 7.68 (t, J = 7.9, 1 H), 7.19 (s, 1 H).

EXAMPLE 408

4-Trifluoromethyl-6-(3,5-dichloro)phenyl-2(1*H*)-quinolinone (Compound **728**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3,5-dichloro)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 2,3-dichlorobenzeneboronic acid. Compound **728** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.46 (s, 1 H), 8.02 (dd, J = 8.7, 1.5, 1 H), 7.82 (s, 1 H), 7.69 (d, J = 1.7, 2 H), 7.65 (d, J = 1.8, 1 H), 7.54 (d, J = 8.6, 1 H), 7.07 (s, 1 H).

EXAMPLE 409

4-Trifluoromethyl-6-(3-fluoro-5-N-hydroxyliminomethyl)phenyl-2(1*H*)-quinolinone (Compound 729, Structure **146** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^3 = 3-fluoro-5-(N-hydroxyliminomethyl)

4-Trifluoromethyl-6-(3-fluoro-5-formylmethylphenyl)-2(1*H*)-quinolinone (Compound **730**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3-fluoro-5-formyl):

This compound was made according to General Procedure XXIV in Example 406 from Compound 308 (Structure 16c of Scheme XXX, where R = H, R^1 = trilfuoromethyl) (500 mg, 1.70 mmol) and 3-fluoro-5-formylbenzeneboronic acid (350 mg, 2.55 mmol, 1.5 equiv). The crude product could not be purified and was used directly in the following step.

4-Trifluoromethyl-6-(3-fluoro-5-(N-hydroxylimino)methylphenyl)-2(1*H*)-quinolinone (Compound 729, Structure 146 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^3 = 3-fluoro-5-(N-hydroxyliminomethyl):

The crude Compound 730 was dissolved in EtOH and treated with hydroxylamine-hydrochloride salt (180 mg, 2.55 mmol, 1.5 equiv) and pyridine (0.2 mL, 2.55 mmol, 1.5 equiv) at room temperature overnight. The crude product was then concentrated, dissolved in EtOAc (200 mL), washed with sat. NH_4Cl (10 mL), water (10 mL), Brine (10 mL), dried ($MgSO_4$), filtered and concentrated. The crude product was then recrystallized from MeOH/EtOAc to afford desired Compound 729 as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.45 (bs, 1 H), 11.54 (s, 1 H), 8.27 (s, 1 H), 8.01 (dd, J = 7.0, 1.7, 1 H), 7.85 (s, 1 H), 7.72 (s, 1 H), 7.55 (d, J = 8.4, 1 H), 7.53 (dd, J = 11.2, 1.5, 1 H), 7.43 (dd, J = 9.8, 1.5, 1 H), 7.06 (s, 1 H).

EXAMPLE 410

4-Trifluoromethyl-6-(3-fluoro-5-cyano)phenyl-2(1*H*)-quinolinone (Compound 731, Structure 146 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^3 = 3-fluoro-5-cyano)

In a 25 mL flask, a solution of Compound **729** (Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3-fluoro-5-(N-hydroxyliminomethyl) in methylene chloride was treated with thionyl chloride (1.1 equiv) at room temperature for 30 min. till the reaction went completion by TLC. The reaction was quenched with K_2CO_3 and extracted with EtOAc. Removal of solvent and chromatography afforded Compound **731** as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.49 (s, 1 H), 8.06 (m, 2 H), 7.93 (dd, J = 10.1, 1.5, 1 H), 7.89 (m, 2 H), 7.55 (d, J = 8.7, 1 H), 7.08 (s, 1 H).

EXAMPLE 411

4-Trifluoromethyl-6-(3-fluoro-5-chloro)phenyl-2(1*H*)-quinolinone (Compound 732, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3-fluoro-5-chloro)

3-Chloro-5-fluorobenzeneboronic acid (Compound **733**, Structure **144** of Scheme XXX, where R^2 = 3-fluoro-5-chloro):

This compound was prepared according to General Procedure XXIII in Example 406 from 1-bromo-3-chloro-5-fluorobenzene (20 g, 0.18 mmol), *n*-BuLi (8.2 M in hexane, 21 mL, 0.18 mmol), and trimethyl borate (60 mL, 0.53 mmol) to give 2,3-difluoro-benzeneboronic acid as a white solid.

4-Trifluoromethyl-6-(3-fluoro-5-chloro)phenyl-2(1*H*)-quinolinone (Compound **732**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3-fluoro-5-chloro):

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and Compound **733**. Compound **732** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.45 (s, 1 H), 8.03 (d, *J* = 8.7, 1 H), 7.58-7.52 (m, 3 H), 7.48 (d, *J* = 8.7, 1 H), 7.07 (s, 1 H).

EXAMPLE 412

4-Trifluoromethyl-6-(4-hydroxymethyl)phenyl-2(1*H*)-quinolinone (Compound 734, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 4-hydroxymethyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 4-hydroxymethylbenzeneboronic acid. Compound **734** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 12.43 (s, 1 H), 7.97 (d, *J* = 8.5, 1 H), 7.82 (s, 1 H), 7.61 (d, *J* = 8.1, 2 H), 7.54 (d, *J* = 8.6, 1 H), 7.44 (d, *J* = 8.1, 2 H), 7.04 (s, 1 H), 5.26 (bs, 1 H), 4.56 (d, *J* = 5.0, 2 H).

EXAMPLE 413

4-Trifluoromethyl-6-(3-acetylphenyl)-2(1*H*)-quinolinone (Compound 735, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3-acetyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and

commercially available 3-acetylbenzeneboronic acid. Compound **735** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.45 (s, 1 H), 8.15 (s, 1 H), 8.04 (d, J = 8.8, 1 H), 8.00 (d, J = 7.8, 1 H), 7.91 (d, J = 8.0, 1 H), 7.86 (s, 1 H), 7.67 (t, J = 7.7, 1 H), 7.58 (d, J = 8.6, 1 H), 7.06 (s, 1 H), 2.66 (s, 3 H).

EXAMPLE 414

4-Trifluoromethyl-6-(4-ethylphenyl)-2(1*H*)-quinolinone (Compound 736, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 4-ethyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 4-ethylbenzeneboronic acid. Compound **736** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.78 (bs, 1 H), 8.00 (s, 1 H), 7.84 (d, J = 8.6, 1 H), 7.53 (d, J = 8.0, 2 H), 7.48 (d, J = 8.6, 1 H), 7.32 (d, J = 8.0, 2 H), 7.13 (s, 1 H), 2.72 (q, J = 7.5, 2 H), 1.29 (t, J = 7.6, 3 H).

EXAMPLE 415

4-Trifluoromethyl-6-(3-ethoxylphenyl)-2(1*H*)-quinolinone (Compound 737, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3-ethoxyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 3-methoxybenzeneboronic acid. Compound **737** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 12.25 (bs, 1 H), 8.02 (s, 1 H), 7.84 (d, J = 8.5, 1 H), 7.53 (d, J = 8.6, 1 H), 7.41 (t, J = 8.0, 1 H), 7.19 (d, J = 6.5, 1 H), 7.14 (m, 2 H), 6.95 (d, J = 8.3, 1 H), 3.89 (s, 3 H).

EXAMPLE 416

4-Trifluoromethyl-6-(3-methylphenyl)-2(1*H*)-quinolinone (Compound 738, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3-methyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 3-methylbenzeneboronic acid. Compound **738** was isolated as a white

solid: ^{1}H NMR (400 MHz, $CDCl_3$) 12.38 (bs, 1 H), 8.01 (s, 1 H), 7.84 (d, J = 8.6, 1 H), 7.54 (d, J = 8.5, 1 H), 7.38 (m, 3 H), 7.22 (d, J = 6.8, 1 H), 7.15 (s, 1 H), 2.46 (s, 3 H).

EXAMPLE 417

4-Trifluoromethyl-6-(3-trifluoromethylphenyl)-2(1*H*)-quinolinone (Compound 739, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3-trifluoromethyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 3-trifluoromethylbenzeneboronic acid. Compound **739** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.46 (bs, 1 H), 8.06 (d, J = 8.6, 1 H), 7.97 (d, J = 6.8, 1 H), 7.93 (s, 1 H), 7.86 (s, 1 H), 7.75 (m, 2 H), 7.57 (8.7, 1 H), 7.07 (s, 1 H).

EXAMPLE 418

4-Trifluoromethyl-6-(3-chlorophenyl)-2(1*H*)-quinolinone (Compound 740, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3-chloro)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 3-chlorobenzeneboronic acid. Compound **740** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.46 (s, 1 H), 8.01 (d, J = 7.0, 1 H), 7.82 (s, 1 H), 7.71 (s, 1 H), 7.62 (d, J = 7.7, 1 H), 7.56-7.47 (m, 3 H), 7.07 (s, 1 H).

EXAMPLE 419

4-Trifluoromethyl-6-(3-fluorophenyl)-2(1*H*)-quinolinone (Compound 741, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3-fluoro)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 3-fluorobenzeneboronic acid. Compound **741** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.46 (s, 1 H), 8.00 (dd, J = 8.5, 1.8, 1 H), 7.84 (s, 1 H), 7.68-7.49 (m, 4 H), 7.24 (t, J = 9.3, 1 H), 7.06 (s, 1 H).

EXAMPLE 420

4-Trifluoromethyl-6-(2-methylphenyl)-2(1*H*)-quinolinone (Compound **742**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 2-methyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 2-methylbenzeneboronic acid. Compound **742** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.42 (s, 1 H), 7.68 (dd, J = 9.6, 1.4, 1 H), 7.53 (m, 2 H), 7.33-7.23 (m, 4 H), 7.04 (s, 1 H), 2.51 (s, 3 H).

EXAMPLE 421

4-Trifluoromethyl-6-(4-formyl)phenyl-2(1*H*)-quinolinone (Compound **743**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 4-formyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 4-formylbenzeneboronic acid. Compound **743** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.49 (s, 1 H), 10.08 (s, 1 H), 8.08 (d, J=10.3, 1 H), 8.04 (d, J = 8.2, 2 H), 7.92 (s, 1 H), 7.91 (d, J = 8.2, 2 H), 7.58 (d, J = 8.6, 1 H), 7.07 (s, 1 H).

EXAMPLE 422

4-Trifluoromethyl-6-(4-tert-butylphenyl)-2(1*H*)-quinolinone (Compound **744**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 4-*tert*-butyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 4-*tert*-butylbenzeneboronic acid. Compound **744** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.40 (s, 1H), 7.95 (d, J = 7.8, 1H), 7.81 (s, 1H), 7.58-7.51 (m, 4H), 7.04 (s, 1H), 1.32 (s, 9H).

EXAMPLE 423

4-Trifluoromethyl-6-(2-methoxyphenyl)-2(1*H*)-quinolinone (Compound **745**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 2-methoxy)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and

commercially available 2-methoxybenzeneboronic acid. Compound **745** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.38 (s, 1 H), 7.81 (s, 1 H), 7.77 (dd, J = 8.6, 1.4, 1 H), 7.49 (d, J = 8.4, 1 H), 7.38 (dt, J = 8.3,1.7, 1 H), 7.34 (dd, J = 7.9, 1.5, 1 H), 7.15 (d, J = 8.1, 1 H), 7.07 (t, J = 7.5, 1 H), 7.02 (s, 1 H), 3.78 (s, 3 H).

EXAMPLE 424

4-Trifluoromethyl-6-(2-fluorophenyl)-2(1*H*)-quinolinone (Compound **746**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 2-fluoro)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 2-fluorobenzeneboronic acid. Compound **746** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.42 (bs, 1 H), 7.85 (d, J = 8.8, 1 H), 7.81 (s, 1 H), 7.55 (m, 2 H), 7.45 (m, 1 H), 7.35 (m, 2 H), 7.04 (s, 1 H).

EXAMPLE 425

4-Trifluoromethyl-6-(4-acetylphenyl)-2(1*H*)-quinolinone (Compound **747**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 4-acetyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 4-acetylbenzeneboronic acid. Compound **747** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.06 (bs, 1 H), 8.06 (m, 3 H), 7.87 (dd, J = 8.7, 1.5, 1 H), 7.69 (d, J = 8.4, 2 H), 7.55 (d, J = 8.6, 1 H), 7.15 (s, 1 H), 2.65 (s, 3 H).

EXAMPLE 426

4-Trifluoromethyl-6-(4-methylphenyl)-2(1*H*)-quinolinone (Compound **748**, Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 4-methyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 4-methylbenzeneboronic acid. Compound **748** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 11.65 (bs, 1 H), 8.00 (s, 1 H), 7.83 (d, J = 8.4, 1 H), 7.49 (m, 3 H), 7.29 (d, J = 8.0, 2 H), 7.13 (s, 1 H), 2.42 (s, 3 H).

EXAMPLE 427

4-Trifluoromethyl-6-(4-fluorophenyl)-2(1*H*)-quinolinone (Compound 749, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 4-fluoro)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 4-fluorobenzeneboronic acid. Compound **749** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.3 (bs, 1 H), 7.94 (d, J = 8.2, 1 H), 7.79 (s, 1 H), 7.69 (dd, J = 8.4, 5.8, 2 H), 7.54 (d, J = 8.6, 1 H), 7.33 (t, J = 8.7, 2 H), 7.04 (s, 1 H).

EXAMPLE 428

4-Trifluoromethyl-6-(4-methoxyphenyl)-2(1*H*)-quinolinone (Compound 750, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 4-methoxy)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 4-methoxybenzeneboronic acid. Compound **750** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.39 (s, 1 H), 7.93 (d, J = 8.5, 1H), 7.77 (s, 1 H), 7.58 (d, J = 8.7, 2 H), 7.52 (d, J = 8.7, 1 H), 7.07 (d, J = 8.7, 2 H), 7.03 (s, 1 H), 3.81 (s, 3 H).

EXAMPLE 429

4-Trifluoromethyl-6-(3,5-bis-trifluoromethyl)phenyl-2(1*H*)-quinolinone (Compound 751, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 3,5-di-trifluoromethyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 3,5-di-trifluorobenzeneboronic acid. Compound **751** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.02 (bs, 1 H), 8.00 (s, 3 H), 7.92 (s, 1 H), 7.84 (dd, J = 7.8, 1.9, 1 H), 7.58 (d, J = 8.5, 1 H), 7.19 (s, 1 H).

EXAMPLE 430

4-Trifluoromethyl-6-(4-trifluoromethoxyphenyl)-2(1*H*)-quinolinone (Compound 752, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 4-trifluoromethoxy)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and

commercially available 4-trifluoromethoxybenzeneboronic acid. Compound **752** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 8.00 (d, J = 8.5, 1 H), 7.83 (s, 1 H), 7.78 (d, J = 8.6, 2 H), 7.56 (d, J = 8.7, 1 H), 7.50 (d, J = 8.5, 2 H), 7.06 (s, 1 H).

EXAMPLE 431

4-Trifluoromethyl-6-(2,4-dichlorophenyl)-2(1*H*)-quinolinone (Compound 753, Structure 145 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 2,4-dichloro)

This compound was made according to General Procedure XXIV in Example 406 from Compound **308** (Structure **16c** of Scheme XXX, where R = H, R^1 = trilfuoromethyl) and commercially available 2,4-dichlorobenzeneboronic acid. Compound **753** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.47 (s, 1 H), 7.77 (d, J = 1.8, 1 H), 7.75 (dd, J = 8.4, 1.3, 1 H), 7.69 (s, 1 H), 7.53 (m, 3 H), 7.06 (s, 1 H).

EXAMPLE 432

3-Fluoro-4-trifluoromethyl-6-(2-fluorophenyl)-2(1*H*)-quinolinone (Compound 754, Structure 145 of Scheme XXX, where R = fluoro, R^1 = trifluoromethyl, R^2 = 2-fluoro)

This compound was made according to General Procedure XXIV in Example 406 from 6-Bromo-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **634**, Structure **16c** of Scheme XXX, where R = fluoro, R^1 = trilfuoromethyl) and commercially available 2-fluorobenzeneboronic acid. Compound **754** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.59 (bs, 1H), 7.86 (s, 1H), 7.72 (d, J = 8.5, 1H), 7.52 (m, 2H), 7.44 (m, 1H), 7.33 (m, 2H).

EXAMPLE 433

3-Fluoro-4-trifluoromethyl-6-(2,4-dichlorophenyl)-2(1*H*)-quinolinone (Compound 755, Structure 145 of Scheme XXX, where R = fluoro, R^1 = trifluoromethyl, R^2 = 2,4-dichloro)

This compound was made according to General Procedure XXIV in Example 406 from Compound **634** (Structure **16c** of Scheme XXX, where R = fluoro, R^1 = trilfuoromethyl) and commercially available 2,4-dichlorobenzeneboronic acid. Compound **755** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.88 (bs, 1H), 7.80 (s, 1H), 7.72 (m, 2H), 7.58 (m, 2H), 7.49 (d, J = 8.2, 1H).

EXAMPLE 434

4-Trifluoromethyl-6-(4-hydroxyphenyl)-2(1*H*)-quinolinone (Compound 756, Structure 146 of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^3 = 4-hydroxy)

This compound was prepared in a similar fashion as that described in Example 211 from Compound **750** (Structure **145** of Scheme XXX, where R = H, R^1 = trifluoromethyl, R^2 = 4-methoxy). Compound **585** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 12.38 (bs, 1H), 9.67 (bs, 1H), 7.89 (d, J = 8.5, 1H), 7.74 (s, 1H), 7.48 (m, 3H), 7.02 (s, 1H), 6.89 (d, J = 8.4, 1H).

EXAMPLE 435

6-Bromo-4-methyl-2(1*H*)-quinolinone (Compound 757, Structure 16c of Scheme XXX, where R = H, R^1 = methyl)

This compound was prepared in a similar fashion as that described in Example 1, General Procedure I by Knorr reaction of 4-bromoaniline and ethyl acetoacetate. Compound **757** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 11.7 (s, 1 H), 7.86 (d, J = 2.1, 1 H), 7.66 (dd, J = 7.5, 2.1, 1 H), 7.27 (d, J = 7.5, 1 H), 6.45 (s, 1 H), 2.41 (s, 3 H).

EXAMPLE 436

4-Methyl-6-(3-methoxyphenyl)-2(1*H*)-quinolinone (Compound 758, Structure 145 of Scheme XXX, where R = H, R^1 = methyl, R^2 = 3-methoxy)

This compound was made according to General Procedure XXIV in Example 406 from Compound **757** (Structure **16c** of Scheme XXX, where R = H, R^1 = methyl) and commercially available 3-methoxybenzeneboronic acid. Compound **758** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.0 (s, 1 H), 7.88 (d, J = 2.0, 1 H), 7.74 (dd, J = 8.5, 2.1, 1 H), 7.51 (d, J = 8.5, 1 H), 7.39 (t, J = 7.9, 1 H), 7.20 (dt, J = 7.9, 1.8, 1 H), 7.14 (t, J = 1.8, 1 H), 6.92 (dt, J = 7.9, 1.8, 1 H), 6.64 (s, 1 H), 2.56 (s, 3 H).

EXAMPLE 437

4-Methyl-6-(3-chlorophenyl)-2(1*H*)-quinolinone (Compound 759, Structure 145 of Scheme XXX, where R = H, R^1 = methyl, R^2 = 3-chloro)

This compound was made according to General Procedure XXIV in Example 406 from Compound **757** (Structure **16c** of Scheme XXX, where R = H, R^1 = methyl) and commercially

available 3-chlorobenzeneboronic acid. Compound **759** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.1 (s, 1 H), 7.83 (d, J = 2.0, 1 H), 7.72 (dd, J = 8.5, 2.1, 1 H), 7.60 (t, J = 7.9, 1 H), 7.55-7.35 (m, 4 H), 6.65 (s, 1 H), 2.58 (s, 3 H).

EXAMPLE 438

4-Methyl-6-(3-chloro-2-methylphenyl)-2(1*H*)-quinolinone (Compound **760**, Structure **145** of Scheme XXX, where R = H, R^1 = methyl, R^2 = 3-chloro-2-methyl).

This compound was made according to General Procedure XXIV in Example 406 from Compound **757** (Structure **16c** of Scheme XXX, where R = H, R^1 = methyl) and commercially available 3-chloro-2-methylbenzeneboronic acid. Compound **760** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 11.70 (s, 1 H), 7.65-7.25 (m, 6 H), 6.45 (s, 1 H), 2.43 (s, 3 H), 2.27 (s, 3 H).

EXAMPLE 439

4-Methyl-6-(2,3-dichlorophenyl)-2(1*H*)-quinolinone (Compound **761**, Structure **145** of Scheme XXX, where R = H, R^1 = methyl, R^2 = 2,3-dichloro)

This compound was made according to General Procedure XXIV in Example 406 from Compound **757** (Structure **16c** of Scheme XXX, where R = H, R^1 = methyl) and commercially available 2,3-dichlorobenzeneboronic acid. Compound **761** was isolated as a white solid: ^{1}H NMR (400 MHz, DMSO-d_6) 11.70 (s, 1 H), 7.75-7.35 (m, 6 H), 6.43 (s, 1 H), 2.45 (s, 3 H).

EXAMPLE 440

4-Methyl-6-(2,4-dichlorophenyl)-2(1*H*)-quinolinone (Compound **762**, Structure **145** of Scheme XXX, where R = H, R^1 = methyl, R^2 = 2,4-dichloro)

This compound was made according to General Procedure XXIV in Example 406 from Compound **757** (Structure **16c** of Scheme XXX, where R = H, R^1 = methyl) and commercially available 2,4-dichlorobenzeneboronic acid. Compound **762** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_6$) 11.00 (s, 1 H), 7.72 (s, 1 H), 7.57 (d, J = 8.5, 1 H), 7.53 (s, 1 H), 7.40-7.30 (m, 3 H), 6.61 (s, 1 H), 2.52 (s, 3 H).

EXAMPLE 441

4-Methyl-6-(2-methylphenyl)-2(1*H*)-quinolinone (Compound 763, Structure 145 of Scheme XXX, where R = H, R^1 = methyl, R^2 = 2-methyl)

This compound was made according to General Procedure XXIV in Example 406 from Compound **757** (Structure **16c** of Scheme XXX, where R = H, R^1 = methyl) and commercially available 2-methylbenzeneboronic acid. Compound **763** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_6$) 11.00 (s, 1 H), 7.62 (s, 1 H), 7.50 (s, 2 H), 7.35-7.27 (m, 4 H), 6.65 (s, 1 H), 2.52 (s, 3 H), 2.30 (s, 3 H).

EXAMPLE 442

4-Trifluoromethyl-6-phenyl-2(1*H*)-quinolinone (Compound 764, Structure 145 of Scheme XXX, where R = H, R^1 = trfluoromethyl, R^2 = H)

This compound was made according to General Procedure I in Example 1 by Knorr reaction of 4-phenylaniline (Structure **147** of Scheme XXX, where R^2 = H) and ethyl 4,4,4-trifluoroacetoaceate. Compound **764** was isolated as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) 11.61 (s, 1 H), 8.05 (s, 1 H), 7.87 (d, J = 8.6, 1 H), 7.61 (d, J = 7.4, 2 H), 7.50 (m, 3 H), 7.43 (t, J = 7.4, 1 H), 7.16 (s, 1 H).

EXAMPLE 443

4-Trifluoromethyl-6-propio-2(1*H*)-quinolinone (Compound 765, Structure 149 of Scheme XXXI, where R = ethyl)

4-Trifluoromethyl-6-propio-2-isopropyloxyquinoline (Compound **766**, Structure **148** of Scheme XXXI, where R = ethyl):

This compound was prepared according to the following General Procedure XXV:

To a solution of Compound **309** (Structure **17** of Scheme XXXI) in THF at –70 °C was added n-BuLi and the mixture was stirred for 10 min. A Weinreb's amide such as N-methyl-N-methoxypropionamide in THF was added to the reaction mixture and the reaction was slowly warmed up to rt and quenched with water. Extraction with EtOAc and washing the organic layer with brine afforded a crude mixture, which was concentrated and chromatographied to give Compound **766**.

4-Trifluoromethyl-6-propio-2(1*H*)-quinolinone (Compound **765**, Structure **149** of Scheme XXXI, where R = ethyl):

Compound **765** was prepared from Compound **766** upon hydrolysis that is described in Example 101 as General procedure XIV. ^{1}H NMR (400 MHz, acetone-d_6) 11.40 (s, 1H), 8.41 (s, 1H), 8.26 (d, *J* = 8.7, 1H), 7.61 (d, *J* = 8.7, 1H), 7.03 (s, 1H), 3.11 (q, *J* = 6.9, 2H), 1.19 (t, *J* = 6.9, 3H).

EXAMPLE 444

4-Trifluoromethyl-6-(1-ethylaminopropyl)-2(1*H*)-quinolinone (Compound **767**, Structure **150** of Scheme XXXI, where R^1 = ethyl, R^2 = H)

To a mixture of Compound **765** (Structure **149** of Scheme XXXI) and ethylamine in methanol were added TFA and $NaCNBH_3$. The reaction mixture was stirred at rt for 1h, quenched with water, extracted with EtOAc and concentrated. Chromatography afforded Compound **767** as white solid. ^{1}H NMR (400 MHz, acetone-d_6) 11.60 (s, 1H), 7.75 (s, 1H), 7.67 (dd, *J* = 8.5, 1.6, 1H) 7.50 (d, *J* = 8.5, 1H), 6.90 (s, 1H), 3.69 (t, *J* = 6.5, 1H), 3.31 (s, 1H), 2.64-2.48 (m, 1H), 2.46-2.38 (m, 1H), 1.81-1.70 (m, 1H), 1.68-1.60 (m, 1H), 1.04 (t, *J* = 7.1, 3H), 0.82 (t, *J* = 7.4, 3H).

EXAMPLE 445

4-Trifluoromethyl-6-(1-N-ethyl-N-methylaminopropyl)-2(1*H*)-quinolinone (Compound **768**, Structure **150** of Scheme XXXI, where R^1 = ethyl, R^2 = methyl)

This compound was prepared from Compound N16 and formaldehyde in a similar fashion as that described in Example 2, General procedure IV as a white solid. ^{1}H NMR (400 MHz, acetone-d_6) 11.42 (s, 1H), 7.64 (s, 1H), 7.61 (d, *J* = 8.5, 1H) 7.51 (d, *J* = 8.5, 1H), 2.54-2.48 (m, 1H), 2.36-2.32 (m, 1H), 2.20 (s, 3H), 2.01-1.95 (m, 1H), 1.79-1.72 (m, 1H), 1.01 (t, *J* = 7.0, 3H), 0.77 (t, *J* = 7.3, 3H).

EXAMPLE 446

4-Trifluoromethyl-6-(1-hydroxy-1-methyl-2-oxopropyl)-2(1*H*)-quinolinone (Compound 769, Structure 152 of Scheme XXXI, where R = methyl, R^1 = acetyl)

4-Trifluoromethyl-6-(1-hydroxy-1-methyl-2,2-dimethoxypropyl)-2-isopropyloxyquinoline (Compound **770**, Structure **151** of Scheme XXXI, R = methyl, R^1 = 1,1-dimethoxyethyl):

This compound was prepared from Compound **309** (Structure **17** of Scheme XXXI) and 3,3-dimethoxy-2-butanone in a similar fashion as that described in Example 330, General procedure XIX.

4-Trifluoromethyl-6-(1-hydroxy-1-methyl-2-oxopropyl)-2(1*H*)-quinolinone (Compound **769**, Structure **152** of Scheme XXXI, where R = methyl, R^1 = acetyl):

This compound was prepared from hydrolysis of Compound **770** in a similar fashion as that described in Example 101, General Procedure XIV as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) 10.72 (s, 1H), 7.96 (s, 1H), 7.68 (d, *J* = 8.9, 1H), 7.50 (d, *J* = 8.9, 1H), 7.13 (s, 1H), 4.62 (s, 1H), 2.12 (d, *J* = 1.9, 3H), 1.8 (s, 1H).

EXAMPLE 447

4-Trifluoromethyl-6-(4,4,4-trifluoro-1(*E*)-butenyl)-2(1*H*)-quinolinone (Compound 771, Structure 153 of Scheme XXXI, where R^2 = H, R^3 = 2,2,2-trilfuoroethyl)

4-Trifluoromethyl-6-(4,4,4-trifluorobutyro)-2-isopropyloxyquinoline (Compound **772**, Structure **148** of Scheme XXXI, where R = 3,3,3-trifluoropropyl):

This compound was prepared in a similar fashion as that described in Example 443, General Procedure XXV from Compound **309** (Structure **17** of Scheme XXXI) and N-methyl-N-methoxybutyramide.

4-Trifluoromethyl-6-(1-hydroxy-4,4,4-trifluorobutyl)-2-isopropyloxyquinoline (Compound **773**, Structure **152** of Scheme XXXI, where R = H, R^1 = 3,3,3-trifluoropropyl):

This compound was prepared in a similar fashion as that described in Example 358, General Procedure XXI from Compound **772**.

4-Trifluoromethyl-6-(4,4,4-trifluoro-1(*E*)-butenyl)-2(1*H*)-quinolinone (Compound **771**, Structure **153** of Scheme XXXI, where R^2 = H, R^3 = 2,2,2-trilfuoroethyl):

This compound was prepared in a similar fashion as that described in Example 101, General Procedure XIV from Compound **773** as the only product. ^{1}H NMR (400 MHz, acetone-d_6) 11.17 (s, 1H), 7.89 (d, J = 8.1, 1H), 7.75 (s, 1H), 7.53 (d, J = 8.6, 1H), 6.96 (s, 1H), 6.89 (d, J = 15.9, 1H), 6.33-6.25 (m, 1H), 3.26-3.17 (m, 1H).

EXAMPLE 448

4-Trifluoromethyl-6-(1-(3,3,3-trifluoropropyl)-1(*E*)-propenyl)-2(1*H*)-quinolinone (Compound **774**, Structure **153** of Scheme XXXI, where R^2 = 3,3,3-trifluoropropyl, R^3 = methyl)

4-Trifluoromethyl-6-(1-ethyl-1-hydroxy-4,4,4-trifluorobutyl)-2-isopropyloxyquinoline (Compound **775**, Structure **151** of Scheme XXXI, where R = ethyl, R^1 = 3,3,3-trifluoropropyl):

To a solution of Compound **772** (Structure **148** of Scheme XXXI, where R = 3,3,3-trifluoropropyl) in THF was added EtMgBr in THF and the reaction mixture was stirred at rt overnight till the starting material was consumed by TLC. The reaction was quenched by water, extracted with EtOAc, washed with brine and concentrated. Chromatography afforded Compound **775** as oil.

4-Trifluoromethyl-6-(1-(3,3,3-trifluoropropyl)-1(*E*)-propenyl)-2(1*H*)-quinolinone (Compound **774**, Structure **153** of Scheme XXXI, where R^2 = 3,3,3-trifluoropropyl, R^3 = methyl):

This compound was prepared in a similar fashion as that described in Example 101, General Procedure XIV from Compound **775** as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) 11.99 (s, 1H), 7.60 (s, 1H), 7.47 (d, J = 8.5, 1H), 7.43 (dd, J = 8.5, 2.0, 1H), 7.13 (s, 1H), 5.76 (q, J = 7.0, 1H), 2.66 (t, J = 8.5, 2H), 2.12-2.05 (m, 2H), 1.66 (d, J = 7.0, 3H).

EXAMPLE 449

4-Trifluoromethyl-6-(1-ethyl-4,4,4-trifluoro-1(*E*)-butenyl)-2(1*H*)-quinolinone (Compound **776**, Structure **153** of Scheme XXXI, R^2 = ethyl, R^3 = 2,2,2-trifluoroethyl) and 4-Trifluoromethyl-6-(1-ethyl-4,4,4-trifluoro-1(*Z*)-butenyl)-2(1*H*)-quinolinone (Compound **777**, Structure **153** of Scheme XXXI, R^2 = ethyl, R^3 = 2,2,2-trifluoroethyl)

Compound **776** was isolated from the hydrolysis of Compound **775**, Structure **151** of Scheme XXXI, where R = ethyl, R^1 = 3,3,3-trifluoropropyl) as that described in Example 448 as the E-isomer. ^{1}H NMR (500 MHz, $CDCl_3$) 11.02 (s, 1H), 7.77 (s, 1H), 7.61 (dd, J = 8.5, 2.0,

1H), 7.39 (s, 1H), 7.34 (d, J = 8.5, 1H), 7.10 (s, 1H), 5.63 (t, J = 7.5, 1H), 3.08-3.02 (m, 2H), 2.57 (q, J = 7.5, 2H), 1.01 (t, J = 7.5, 3H).

Compound **777** was isolated from the hydrolysis of Compound **775**, Structure **151** of Scheme XXXI, where R = ethyl, R^1 = 3,3,3-trifluoropropyl) as that described in Example 448 as the Z-isomer. ^{1}H NMR (500 MHz, $CDCl_3$) 11.60 (s, 1H), 7.56 (s, 1H), 7.37 (s, 2H), 7.09 (*s*, 1H), 5.52-5.57 (m, 1H), 2.71-2.66 (m, 2H), 2.45-2.40 (m, 2H), 1.02 (t, J = 7.4, 3H).

EXAMPLE 450

2-Chloro-4-trifluoromethyl-6-(bis-N,N-2,2,2-trifluoroethyl)aminoquinoline (Compound 778, Structure 154 of Scheme XXXII, where R^1 = R^2 = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **223** (Structure **7** of Scheme XXXII, where R^1 = R^2 = 2,2,2-trifluoroethyl) from the following procedure.

To the quinolinone (20.0 mg, 0.05 mmol) in toluene (0.25 mL) was added $POCl_3$ (30.0 microlitres, 0.30 mmole, 6 equiv). The resulting reaction mixture was heated to 110 °C for 4-8 h, cooled to rt, diluted with EA (25 mL) and washed with 20% KOH (2 x 25 mL). The organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the resulting oil by flash chromatography (EtOAc:hexane mixtures) afforded the 2-chloro-6-amino-quinolines.

Compound **778** was isolated as yellow solid; ^{1}H NMR ($CDCl_3$, 500 MHz) 8.06 (d, J = 9.8, 1H), 7.66 (s, 1H), 7.53 (dd, J = 2.4, 9.3, 1H), 7.41 (bs, 1H), 4.21 (q, J = 8.3, 4H).

EXAMPLE 451

2-Methoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound 779, Structure 155 of Scheme XXXII, where R = methoxy, R^1 = R^2 = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **778** from the following General Procedure XXVI:

A mixture of Compound **778** (Structure **154** of Scheme XXXII, where R^1 = R^2 = 2,2,2-trifluoroethyl) NaOMe (1.5 equiv) in methanol was heated at reflux for 2h till the starting material was consumed by TLC. The reaction was quenched by water and a solid was precipitated. Filtration followed washing with methanol afforded the 2-methoxyquinoline in 70-90% yield.

Compound **779** was isolated as a white solid. ^{1}H NMR (400 MHz, acetone-d_6) 7.89 (d, J = 9.3, 1H) 7.77 (dd, J = 9.1, 2.3, 1H), 7.49 (s, 1H), 7.30 (s, 1H), 4.51 (q, J = 8.6, 4H), 4.05 (s, 3H).

EXAMPLE 452

2-Isopropyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **780**, Structure **155** of Scheme XXXII, where R = isopropyloxy, $R^1 = R^2$ = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **223** in a similar fashion as that described in Example 101, General Procedure XII as yellow oil. ^{1}H NMR (400 MHz, acetone-d_6) 7.71 (d, J = 9.3, 1H) 7.61 (dd, J = 9.3, 2.8, 1H), 7.35 (s, 1H), 7.08 (s, 1H), 5.40-5.34 (m, 1H), 4.36 (q, J = 8.7, 4H), 1.25 (d, J = 6.2, 6H).

EXAMPLE 453

2-Ethoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **781**, Structure **155** of Scheme XXXII, where R = ethoxy, $R^1 = R^2$ = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **778** (Structure **154** of Scheme XXXII, where $R^1 = R^2$ = 2,2,2-trifluoroethyl) in a similar fashion as that described in Example 451, General Procedure XXVI as yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) 7.83 (d, J = 10.2, 1 H), 7.39-7.37 (m, 2 H), 7.21 (s, 1 H), 4.51 (q, J = 6.8, 2 H), 4.14 (q, J_{H-F} = 8.8, 4 H), 1.44 (t, J = 6.8, 3 H).

EXAMPLE 454

2-Acetyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **782**, Structure **155** of Scheme XXXII, where R = acetyloxy, $R^1 = R^2$ = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **223** and acetic anhydride by the following General Procedure XXVII.

To a solution of 220 mg (0.46 mmol) of Compound **223** (Structure 7 of Scheme XXXII, where $R^1 = R^2$ =2,2,2-trifluoroethyl) in 10 mL THF in a 100 mL rb flask was added Et_3N (0.3 mL, 2.5 mmol) followed by Ac_2O (0.3 mL, 4 mmol) and DMAP (5 mg, 0.01 eq). The mixture was stirred at rt for 3 h and then 50 mL water was added. Extracted with 50 mL EtOAc, and the organic layer was quickly washed with 2.5 N HCl (2 x 50 mL), sat $NaHCO_3$, and brine, and dried over $MgSO_4$. Concentration and purification by chromatography (silica gel, hex : EtOAc 5:1)

afforded 192 mg of Compound **782** as yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) 8.02(d, J = 9.8, 1 H), 7.51 (dd, J = 9.3, 2.9, 1 H), 7.49 (s, 1 H), 7.45 (s, 1 H), 4.20 (q, J_{H-F} = 8.8, 4 H), 2.41 (s, 3 H).

EXAMPLE 455

2-(2-Dimethylamino)ethoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound 783, Structure 155 of Scheme XXXII, where R = 2-dimethylaminoethoxy, R^1 = R^2 = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **778** (Structure **154** of Scheme XXXII, where R^1 = R^2 = 2,2,2-trifluoroethyl) and 2-dimethylaminoethanol in a similar fashion as that described in Example 451, General Procedure XXVI as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) 7.83 (d, J = 10.4, 1H), 7.30-7.39 (m, 2H), 7.28 (s, 1H), 4.57 (t, J = 5.5, 2H), 4.14 (q, J = 8.4, 2H), 2.76 (t, J = 5.5, 2H), 2.36 (s, 6H).

EXAMPLE 456

2-Isobutyryloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound 784, Structure 155 of Scheme XXXII, where R = isobutyryloxy, R^1 = R^2 = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **223** (Structure **7** of Scheme XXXII, where R^1 = R^2 = 2,2,2-trifluoroethyl) and isobutyric anhydride in a similar fashion as that described in Example 454, General Procedure XXVII as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) 8.04 (d, J = 9.3, 1 H), 7.50 (dd, J = 9.3, 2.9, 1 H), 7.45 (s, 1 H), 7.44 (s, 1 H), 4.20 (q, J_{H-F} = 8.8, 4 H), 2.95-2.89 (m, 1 H), 1.39 (d, J = 6.8, 6 H).

EXAMPLE 457

2-(2,2-Dimethyl)propyryloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)-aminoquinoline (Compound 785, Structure 155 of Scheme XXXII, where R = *tert*-butyryloxy, R^1 = R^2 = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **223** (Structure **7** of Scheme XXXII, where R^1 = R^2 = 2,2,2-trifluoroethyl) and valeric anhydride in a similar fashion as that described in Example 454, General Procedure XXVII as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) 8.05 (d, J = 9.3, 1 H), 7.50 (dd, J = 9.3, 2.9, 1 H), 7.45 (s, 1 H), 7.42 (s, 1 H), 4:20 (q, J_{H-F} = 8.3, 4 H), 1.45 (s, 9 H).

EXAMPLE 458

2-N,N-Dimethylcarbamyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)-aminoquinoline (Compound 786, Structure 155 of Scheme XXXII, where R = dimethylaminocarbonyloxy, R^1 = R^2 = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **223** (Structure 7 of Scheme XXXII, where R^1 = R^2 = 2,2,2-trifluoroethyl) and dimethylcarbamyl chloride in a similar fashion as that described in Example 454, General Procedure XXVII as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) 8.02 (d, J = 9.3, 1 H), 7.55 (s, 1 H), 7.49 (dd, J = 9.3, 2.9, 1 H), 7.44 (s, 1 H), 4.19 (q, J_{H-F} = 8.3, 4 H), 3.18 (s, 3 H), 3.06 (s, 3 H).

EXAMPLE 459

2-Cyano-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound 787, Structure 155 of Scheme XXXII, where R = cyano, R^1 = R^2 = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **778** (Structure **154** of Scheme XXXII, where R^1 = R^2 = 2,2,2-trifluoroethyl) in a similar fashion as that described in Example 451, General Procedure XXVI as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 8.21 (d, J = 9.8, 1H), 7.92 (s, 1H), 7.63 (dd, J = 2.9, 9.8, 1H), 7.42 (s, 1H), 4.27 (q, J = 8.4, 4H).

EXAMPLE 460

4-Trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone oxime (Compound 788, Structure 156 of Scheme XXXII, where R = H, R^1 = R^2 = 2,2,2-trifluoroethyl)

This compound was prepared from Compound **223** (Structure 7 of Scheme XXXII, where R^1 = R^2 = 2,2,2-trifluoroethyl) as yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) 11.20-11.40 (bs, 1H), 7.72 (s, 1H), 7.36 (d, J = 10.2, 1H), 7.28-7.31 (m, 2H), 4.11 (q, J = 8.3, 4H).

EXAMPLE 461

6-(N-2,2,2-Trifluoroethyl-N-nitroso)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 789, Structure 157 of Scheme XXXIII, where R = 2,2,2-trifluoroethyl)

A 100 mL rb flask was charged with a solution of Compound **209** (Structure **7a** of Scheme XXXIII, where R = 2,2,2-trifluoroethyl) (410 mg, 1.32 mmol) in 15 mL conc. HCl and cooled in an ice bath. A solution of $NaNO_2$ (170 mg, 2.5 mmol, 2 eq) in 5 mL water was added dropwise in 20 min and the mixture was stirred in an ice bath for 2 h, then 10 mL water was

added and the solids were filtered and washed with water to give Compound 789 as white solid. ^{1}H NMR (500 MHz, acetone-d_6) 11.4 (bs, 1 H), 8.01-7.98 (m, 2 H), 7.75 (d, J = 9.3, 1 H), 7.08 (s, 1 H), 5.06 (q, $J_{H\text{-}F}$ = 9.3, 2 H).

EXAMPLE 462

6-(N-Isobutyl-N-nitroso)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 790, Structure 157 of Scheme XXXIII, where R = isobutyl)

This compound was prepared in a similar fashion as that described in Example 461 from Compound **206** (Structure **7a** of Scheme XXXIII, where R = isobutyl) and isolated as white solid. ^{1}H NMR (500 MHz, $CDCl_3$) 12.0 (bs, 1 H), 7.94 (dd, J = 9.3, 2.0, 1 H), 7.88 (s, 1 H), 7.56 (d, J = 9.3, 1 H), 7.18 (s, 1 H), 3.95 (d, J = 7.3, 2 H), 2.05-2.00 (m, 1 H), 0.88 (d, J = 6.8, 6 H).

EXAMPLE 463

6-(N-Isobutyl-N-nitroso)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 791, Structure 158 of Scheme XXXIII, where R = 2,2,2-trifluoroethyl, R^1 = H, R^2 = isopropyl)

Compound **789** (Structure **157** of Scheme XXXIII, where R = 2,2,2-trifluoroethyl) was dissolved in a mixture of EtOH (15 mL) and HOAc (10 mL) in a 100 mL rb flask, cooled in an ice bath, and zinc dust (0.5 g, 7.7 mmol, 6 eq) was added in small portions in 20 min. The bright yellow suspension was stirred at rt for 16 h, filtered and rinsed with EtOAc (50 mL) and water (50 mL). 20 mL brine was added and the layers were separated. The water layer was extracted with 50 mL EtOAc, and the combined organic layers were washed with brine (50 mL), and dried over $MgSO_4$. Concentration and purification by chromatography (Silica gel, hex : EtOAc 3:1 to 1:1 gradient) afforded an inseparable mixture of starting material and hydrazine, that was used in the next step.

To a solution of the above mixture (12 mg, 0.04 mmol) in 5 mL TFA in a 100 mL rb flask was added acetone (0.2 mL, excess) and the mixture was stirred at rt for 6 h. $NaCNBH_3$ (200mg, 3.3 mmol) was added in portions over a 2 hour period, and the mixture was stirred at rt for 16 h. 20 mL water was slowly added and the water layer was extracted with EtOAc (3 x 25 mL). The combined org. layers were washed with brine and dried over $MgSO_4$. Concentration in vacuo and purification by column chromatography (Silica gel, hex : EtOAc 4:1 to 2:1 gradient) afforded Compound **791** as yellow solid. ^{1}H NMR (500 MHz, DMSO-d_6) 11.5 (bs, 1 H), 7.39-

7.37 (m, 2 H), 7.31 (d, J = 9.8, 1 H), 7.08 (s, 1 H), 4.09 (q, J = 8.8, 2 H), 3.77 (s, 1 H), 3.25-3.20 (m, 1 H), 1.06 (d, J = 6.3, 6 H).

EXAMPLE 464

6-(4,5-Dihydro-3-methyl-1-pyrazoly)-4-trifluoromethylquinolin-2(1*H*)-one (Compound 792, Structure 160 of Scheme XXXIII, where R^1 = methyl, R^2 = H)

6-Hydrazino-4-trifluoromethylquinolin-2(1*H*)-one (Compound **793**, Structure **159** of Scheme XXXIII)

In a 250 mL rb flask a suspension of Compound **200** (structure **3** of Scheme XXXIII) (2.28 g, 10 mmol) in 10 mL conc. HCl was cooled to –1°C and a solution of $NaNO_2$ (0.40 g, 12 mmol) in water (5 mL) was added dropwise in 20 min. The dark yellow suspension was stirred at –1°C for 1 h and then a solution of $SnCl_2$. $2H_2O$ (5.2 g, 15 mmol) in conc HCl (10 mL) was added dropwise in 10 min. The light yellow suspension of Compound **793** was stirred at –1°C for 2h and then used directly or kept in a refrigerator at –1°C until it was used (the crude compound can be stored for at least one month without decomposition).

6-(4,5-Dihydro-3-methyl-1-pyrazoly)-4-trifluoromethylquinolin-2(1*H*)-one (Compound **792**, Structure **160** of Scheme XXXIII, where R^1 = methyl, R^2 = H)

This compound was prepared by condensation of Compound **793** and 1-buten-3-one as yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) 10.2 (bs, 1 H), 7.55 (dd, J = 8.8, 2.4, 1 H), 7.21 (d, J = 8.8, 1 H), 7.11 (bs, 1 H), 7.05 (s, 1 H), 3.72 (t, J = 10.0, 2 H), 2.90 (t, J = 10.2, 2 H), 2.11 (s, 3 H).

EXAMPLE 465

(±)-6-(4,5-Dihydro-3-ethyl-5-methyl-1-pyrazoly)-4-trifluoromethylquinolin-2(1*H*)-one (Compound 794, Structure 160 of Scheme XXXIII, where R^1 = ethyl, R^2 = methyl)

This compound was prepared from the condensation of Compound **793** (Structure **159** of Scheme XXXIII) and 2-hexen-4-one as yellow solid. ^{1}H NMR (500 MHz, DMSO-d_6) 12.1 (bs, 1 H), 7.41 (dd, J = 8.8, 2.4, 1 H), 7.34 (d, J = 8.8, 1 H), 7.21 (bs, 1 H), 6.92 (s, 1 H), 4.37-4.28 (m, 1 H), 3.12 (dd, J = 17.1, 10.2, 1 H), 2.53 (dd, J = 17.1, 4.9, 1 H), 2.37 (q, J = 7.3, 2 H), 1.12 (t, J = 7.3, 3 H), 1.12 (d, J = 5.9, 3 H).

EXAMPLE 466

6-(N-Acetyl-N-dimethylimino)amino-4-trifluoromethylquinolin-2(1*H*)-one (Compound 795, Structure 161 of Scheme XXXIII)

A mixture of Compound **793** (Structure **159** of Scheme XXXIII) and acetic acid in acetone was heated in a sealed tube at 100 °C for 2h. The reaction mixture was concentrated and chromatographied to afford Compound **795** as major product as yellow solid. ^{1}H NMR (500 MHz, DMSO-d_6) 12.5 (bs, 1 H), 7.79 (dd, J = 9.3, 2.4, 1 H), 7.65 (s, 1 H), 7.54 (d, J = 9.3, 1 H), 7.08 (s, 1 H), 2.22 (s, 3 H), 2.14 (s, 3 H), 1.94 (s, 3 H).

Steroid Receptor Activity

Utilizing the "cis-trans" or "co-transfection" assay described by Evans et al., Science, 240:889-95 (May 13, 1988), the disclosure of which is herein incorporated by reference, the compounds of the present invention were tested and found to have strong, specific activity as both agonists, partial agonists and antagonists of AR. This assay is described in further detail in U.S. Patent Nos. 4,981,784 and 5,071,773, the disclosures of which are incorporated herein by reference.

The co-transfection assay provides a method for identifying functional agonists and partial agonists which mimic, or antagonists which inhibit, the effect of native hormones, and quantifying their activity for responsive IR proteins. In this regard, the co-transfection assay mimics an *in vivo* system in the laboratory. Importantly, activity in the co-transfection assay correlates very well with known *in vivo* activity, such that the co-transfection assay functions as a qualitative and quantitative predictor of a tested compounds *in vivo* pharmacology. See, e.g., T. Berger et al. 41 *J. Steroid Biochem. Molec. Biol.* 773 (1992), the disclosure of which is herein incorporated by reference.

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly

luciferase (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be conveniently measured, e.g., by increasing luciferase production, which reflects compound-dependent, IR-mediated increases in reporter transcription. To detect antagonists, the co-transfection assay is carried out in the presence of a constant concentration of an agonist to the target IR (e.g., progesterone for PR) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., luciferase production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

The activity of selected steroid receptor modulator compounds of the present invention were evaluated utilizing the co-transfection assay, and in standard IR binding assays, according to the following illustrative Examples.

EXAMPLE 467

Co-transfection assay

CV-1 cells (African green monkey kidney fibroblasts) were cultured in the presence of Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% charcoal resin-stripped fetal bovine serum then transferred to 96-well microtiter plates one day prior to transfection.

To determine AR agonist and antagonist activity of the compounds of the present invention, the CV-1 cells were transiently transfected by calcium phosphate coprecipitation according to the procedure of Berger et al., 41 *J. Steroid Biochem. Mol. Biol.*, 733 (1992) with the following plasmids: pShAR (5 ng/well), MTV-LUC reporter (100 ng/well), pRS-ß-Gal (50

ng/well) and filler DNA (pGEM; 45 ng/well). The receptor plasmid, pRShAR, contains the human AR under constitutive control of the SV-40 promoter, as more fully described in *J.*A. Simental et al., "Transcriptional activation and nuclear targeting signals of the human androgen receptor", 266 *J. Biol. Chem.*, 510 (1991).

The reporter plasmid, MTV-LUC, contains the cDNA for firefly luciferase (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing an androgen response element. See e.g, Berger et al. supra. In addition, pRS-ß-Gal, coding for constitutive expression of E. coli ß-galactosidase (ß-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

Six hours after transfection, media was removed and the cells were washed with phosphate-buffered saline (PBS). Media containing reference compounds (i.e. progesterone as a PR agonist, mifepristone ((11beta,17beta)-11-[4-(dimethylamino)phenyl]-17-hydroxy-17-(1-propynyl)estra-4,9-dien-3-one: RU486; Roussel Uclaf) as a PR antagonist; dihydrotestosterone (DHT; Sigma Chemical) as an AR agonist and 2-OH-flutamide (the active metabolite of 2-methyl-N-[4-nitro-3-(trifluoromethyl)phenyl]pronanamide; Schering-Plough) as an AR antagonist; estradiol (Sigma) as an ER agonist and ICI 164,384 (N-butyl-3,17-dihydroxy-N-methyl-(7-alpha,17-beta)-estra-1,3,5(10)-triene-7-undecanamide; ICI Americas) as an ER antagonist; dexamethasone (Sigma) as a GR agonist and RU486 as a GR antagonist; and aldosterone (Sigma) as a MR agonist and spironolactone ((7-alpha-[acetylthio]-17-alpha-hydroxy-3-oxopregn-4-ene-21-carboxylic acid gamma-lactone; Sigma) as an MR antagonist) and/or the modulator compounds of the present invention in concentrations ranging from 10^{-12} to 10^{-5} M were added to the cells. Three to four replicates were used for each sample. Transfections and subsequent procedures were performed on a Biomek 1000 automated laboratory work station.

After 40 hours, the cells were washed with PBS, lysed with a Triton X-100-based buffer and assayed for LUC and ß-Gal activities using a luminometer or spectrophotometer, respectively. For each replicate, the normalized response (NR) was calculated as:

LUC response/ß-Gal rate

where ß-Gal rate = ß-Gal$\cdot 1 \times 10^{-5}$/ß-Gal incubation time.

The mean and standard error of the mean (SEM) of the NR were calculated. Data was plotted as the response of the compound compared to the reference compounds over the range of the dose-response curve. For agonist experiments, the effective concentration that produced 50% of the maximum response (EC_{50}) was quantified. Agonist efficacy was a function (%) of LUC expression relative to the maximum LUC production by the reference agonist for PR, AR, ER, GR or MR. Antagonist activity was determined by testing the amount of LUC expression in the presence of a fixed amount of DHT as an AR agonist and progesterone as a PR agonist at the EC_{50} concentration. The concentration of test compound that inhibited 50% of LUC expression induced by the reference agonist were quantified (IC_{50}). In addition, the efficacy of antagonists was determined as a function (%) of maximal inhibition.

<u>IR Binding assay</u>

<u>AR Binding</u>: For the whole cell binding assay, COS-1 cells in 96-well microtiter plates containing DMEM-10% FBS were transfected as described above with the following plasmid DNA: pRShAR (2 ng/well), pRS-ß-Gal (50 ng/well) and pGEM (48 ng/well). Six hours after transfection, media was removed, the cells were washed with PBS and fresh media was added. The next day, the media was changed to DMEM-serum free to remove any endogenous ligand that might be complexed with the receptor in the cells.

After 24 hours in serum-free media, either a saturation analysis to determine the K_d for tritiated dihydrotestosterone (^{3}H-DHT) on human AR or a competitive binding assay to evaluate the ability of test compounds to compete with ^{3}H-DHT for AR was performed. For the saturation analysis, media (DMEM-0.2% CA-FBS) containing ^{3}H-DHT (in concentrations ranging from 12 nM to 0.24 nM) in the absence (total binding) or presence (non-specific binding) of a 100-fold molar excess of unlabeled DHT were added to the cells. For the competitive binding assay, media containing 1 nM ^{3}H-DHT and test compounds in concentrations ranging from 10^{-10} to 10^{-6} M were added to the cells. Three replicates were used for each sample. After three hours at 37°C, an aliquot of the total binding media at each concentration of ^{3}H-DHT was removed to estimate the amount of free ^{3}H-DHT. The remaining media was removed, the cells were washed three times with PBS to remove unbound ligand, and cells were lysed with a Triton X-100-based buffer. The lysates were assayed for amount of

bound ^{3}H-DHT and ß-Gal activity using a scintillation counter or spectrophotometer, respectively.

For the saturation analyses, the difference between the total binding and the nonspecific binding, normalized by the ß-Gal rate, was defined as specific binding. The specific binding was evaluated by Scatchard analysis to determine the K_d for ^{3}H-DHT. See e.g., D. Rodbard, "Mathematics and statistics of ligand assays: an illustrated guide" In: *J.* Langon and *J.J.* Clapp, eds., *Ligand Assay*, Masson Publishing U.S.A., Inc., New York, pp. 45-99, (1981), the disclosure of which is herein incorporated by reference. For the competition studies, the data was plotted as the amount of ^{3}H-DHT (% of control in the absence of test compound) remaining over the range of the dose-response curve for a given compound. The concentration of test compound that inhibited 50% of the amount of ^{3}H-DHT bound in the absence of competing ligand was quantified (IC_{50}) after log-logit transformation. The K_i values were determined by application of the Cheng-Prusoff equation to the IC_{50} values, where:

$$K_i = \frac{IC_{50}}{(1+[^3\text{H-DHT}])/K_d \text{ for } ^3\text{H-DHT}}$$

After correcting for non-specific binding, IC_{50} values were determined. The IC_{50} value is defined as the concentration of competing ligand needed to reduce specific binding by 50%. The IC_{50} value was determined graphically from a log-logit plot of the data. The K_i values were determined by application of the Cheng-Prusoff equivuation to the IC_{50} values, the labeled ligand concentration and the K_d of the labeled ligand.

The agonist, antagonist and binding activity assay results of selected androgen receptor modulator compounds of present invention and the standard reference compounds on AR, as well as the cross-reactivity of selected compounds on the PR, ER, MR and GR receptors, are shown in Tables 1-2 below. Efficacy is reported as the percent maximal response observed for each compound relative to the reference agonist and antagonist compounds indicated above. Also reported in Tables 1-2 for each compound is its antagonist potency or IC_{50} (which is the concentration (nM), required to reduce the maximal response by 50%), its agonist potency or EC_{50} (nM).

Table 1: Cotransfection and competitive binding data of selected androgen receptor modulator compounds of present invention and the reference agonist compound, dihydrotestosterone (DHT), and reference antagonists compound, 2-hydroxyflutamide (Flut) and Casodex (Cas), on AR.

Cmpd	AR Agonist CV-1 Cells		AR Antagonist CV-1 Cells		AR Binding
No.	Efficacy (%)	Potency (nM)	Efficacy (%)	Potency (nM)	K_i (nM)
204	34	2022	72	27	54
218	78	2.0	na	na	4.4
219	73	1.3	na	na	50
220	68	1280	54	29	222
221	114	23	na	na	147
222	81	2.2	na	na	6.3
223	95	0.15	na	na	1.0
224	108	41	na	na	206
225	90	0.4	na	na	0.9
227	na	na	73	14	38
232	55	3.4	na	na	7.6
238	77	5.3	na	na	17
239	83	2.0	na	na	7.4
241	73	2.9	na	na	30
242	66	2.8	na	na	32
246	115	0.35	na	na	7.1
254	78	0.90	na	na	12
255	135	25	na	na	67
259	97	1.9	na	na	6.3

Cmpd	AR Agonist CV-1 Cells		AR Antagonist CV-1 Cells		AR Binding
No.	Efficacy (%)	Potency (nM)	Efficacy (%)	Potency (nM)	K_i (nM)
262	58	5.9	na	na	29
269	85	11	na	na	14
272	na	na	67	7.0	> 1000
274	67	1.6	na	na	1.4
280	78	2.2	na	na	2.4
285	111	1.0	na	na	6.2
287	34	8.3	53	4.1	> 1000
290	37	32	50	50	> 1000
295	30	50	49	3.6	86
297	43	22	43	3.2	58
307	na	na	43	3.2	61
311	42	143	38	13	12
314	83	5.3	na	na	4.6
328	93	1.7	na	na	48
330	81	3.9	na	na	55
331	44	21	42	5.7	> 1000
332	121	14	na	na	19
341	na	na	85	15	277
347	na	na	89	59	970
348	na	na	81	24	62
350	73	29	na	na	165
351	79	23	na	na	31
352	113	12	ma	na	25
365	36	55	43	14	124
366	na	na	85	31	> 1000

Cmpd	AR Agonist CV-1 Cells		AR Antagonist CV-1 Cells		AR Binding
No.	Efficacy (%)	Potency (nM)	Efficacy (%)	Potency (nM)	K_i (nM)
374	77	2.2	na	na	6.2
377	89	0.45	na	na	1.4
381	72	1.8	na	na	7.8
423	57	86	na	na	22
426	93	45	na	na	28
432	96	8.0	na	na	32
433	120	6.4	na	na	1.5
444	83	73	na	na	26
445	104	26	na	na	5.8
449	83	16	na	na	8.4
457	85	3.0	na	na	3.2
474	73	0.60	na	na	1.8
490	113	12	na	na	12
501	110	5.8	na	na	16
513	na	na	84	26	37
514	na	na	87	55	79
520	na	na	76	58	36
523	29	1000	62	24	16
526	na	na	89	43	161
528	36	1300	59	26	nd
532	na	na	85	73	159
535	na	na	76	60	> 1000
536	na	na	76	28	188
559	na	na	92	122	118
571	na	na	69	14	71

Cmpd	AR Agonist CV-1 Cells		AR Antagonist CV-1 Cells		AR Binding
No.	Efficacy (%)	Potency (nM)	Efficacy (%)	Potency (nM)	K_i (nM)
581	39	65	23	5000	24
582	na	na	92	26	43
602	na	na	85	27	45
615	23	2800	82	48	56
616	na	na	92	17	15
630	30	221	67	13	109
632	na	na	75	36	112
633	33	38	51	7.5	97
645/646	48	848	68	4.1	36
647	42	233	64	31	81
655	na	na	70	70	> 1000
659	na	na	70	44	40
667	na	na	89	27	7.4
675/676	na	na	93	57	192
689	na	na	89	40	132
694	25	935	90	64	> 1000
698	na	na	84	17	32
721	na	na	85	32	> 1000
725	na	na	87	79	>1000
737	na	na	92	89	>1000
738	na	na	91	27	>1000
741	na	na	92	27	322
753	na	na	76	51	74
758	na	na	94	87	3.6
762	na	na	81	63	nd

Cmpd	AR Agonist CV-1 Cells		AR Antagonist CV-1 Cells		AR Binding
No.	Efficacy (%)	Potency (nM)	Efficacy (%)	Potency (nM)	K_i (nM)
764	na	na	87	30	16
HO-Flut	na	na	83	25	34
Casodex	na	na	81	201	117
DHT	100	4.3	na	na	1.7

na = not active (i.e. efficacy of <20 and potency of >10,000); nd = not determined.

<u>Table 2: Co-transfection and competitive binding data for selective progesterone receptor modulator compounds of present invention and the reference agonist compound, progesterone (Prog), and reference antagonists compound, RU486 on PR.</u>

Cmpd	PR Agonist CV-1 Cells		PR Antagonist CV-1 Cells		PR Binding
No.	Efficacy (%)	Potency (nM)	Efficacy (%)	Potency (nM)	K_i (nM)
242	na	na	95	200	70
251	na	na	91	747	930
473	na	na	55	880	508
631	na	na	75	796	136
667	na	na	89	70	144
671	na	na	62	200	> 1000
689	105	2700	47	35	23
695	na	na	90	20	203
697	na	na	58	316	> 1000
725	na	na	92	149	400
727	na	na	90	108	161

Cmpd	PR Agonist CV-1 Cells		PR Antagonist CV-1 Cells		PR Binding
731	na	na	89	64	154
735	na	na	84	326	915
Prog	100	2.9	na	na	3.5
ZK299	na	na	95	2.2	18

na = not active (i.e. efficacy of <20 and potency of >10,000)

Pharmacological and Other Applications

As will be discernible to those skilled in the art, the androgen or progesterone receptor modulator compounds of the present invention can be readily utilized in pharmacological applications where AR or PR antagonist or agonist activity is desired, and where it is desired to minimize cross reactivities with other steroid receptor related IRs. In vivo applications of the invention include administration of the disclosed compounds to mammalian subjects, and in particular to humans.

The following Example provides illustrative pharmaceutical composition formulations:

EXAMPLE 468

Hard gelatin capsules are prepared using the following ingredients:

	Quantity (mg/capsule)
COMPOUND 219	140
Starch, dried	100
Magnesium stearate	10
Total	250 mg

The above ingredients are mixed and filled into hard gelatin capsules in 250 mg quantities.

A tablet is prepared using the ingredients below:

	Quantity (mg/capsule)
COMPOUND 219	140
Cellulose, microcrystalline	200
Silicon dioxide, fumed	10
Stearic acid	10
Total	350 mg

The components are blended and compressed to form tablets each weighing 360 mg.

Tablets, each containing 60 mg of active ingredient, are made as follows:

	Quantity (mg/capsule)
COMPOUND 219	60
Starch	45
Cellulose, microcrystalline	
Polyvinylpyrrolidone (PVP)	35
(as 10% solution in water)	4
Sodium carboxymethyl starch (SCMS)	4.5
Magnesium stearate	0.5
Talc	1.0
Total	150 mg

The active ingredient, starch, and cellulose are passed through a No. 45 mesh U.S. sieve and mixed thoroughly. The solution of PVP is mixed with the resultant powders, which are then passed through a No. 14 mesh U.S. sieve. The granules so produced are dried at 50^{o} C and passed through a No. 18 mesh U.S. sieve. The SCMS, magnesium stearate, and talc, previously passed through a No. 60 mesh U.S. sieve, and then added to the granules which, after mixing, are compressed on a tablet machine to yield tablets each weighing 150 mg.

Suppositories, each containing 225 mg of active ingredient, may be made as follows:

COMPOUND **219**	225 mg
Saturated fatty acid glycerides	2,000 mg
Total	2,225 mg

The active ingredient is passed through a No. 60 mesh U.S. sieve and suspended in the saturated fatty acid glycerides previously melted using the minimum heat necessary. The mixture is then poured into a suppository mold of normal 2g capacity and allowed to cool.

An intravenous formulation may be prepared as follows:

COMPOUND **219**	100 mg
Saturated fatty acid glycerides	1,000 mL
Total	100 mL

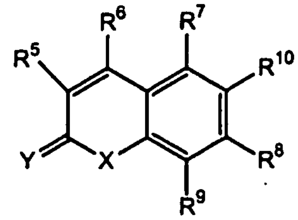
The compound is dissolved in the glycerol and then the solution is slowly diluted with isotonic saline. The solution of the above ingredients is then administered intravenously at a rate of 1 mL per minute to a patient.

While description of the preferred embodiments and processing conditions have been provided, the scope of the invention is not to be limited thereto or thereby. Various modifications and alterations of the present invention will be apparent to those skilled in the art without departing from the scope and spirit of the present invention.

The invention is further described below in the form of non-limiting enumerated embodiments.

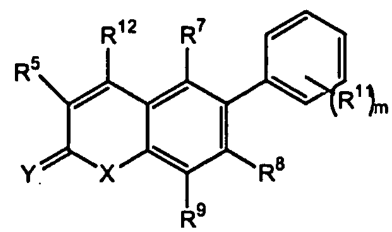
What is claimed is:

1. A compound having the formula:



(I)

OR



(II)

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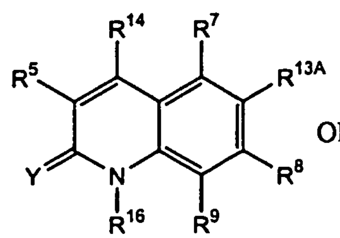

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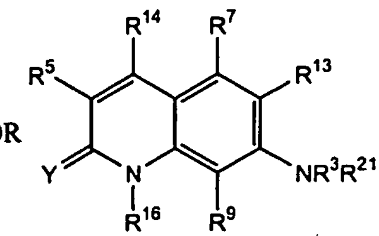

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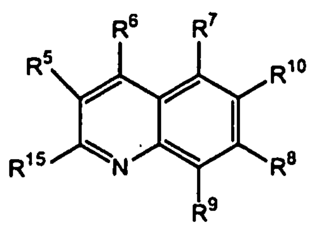

(IV)

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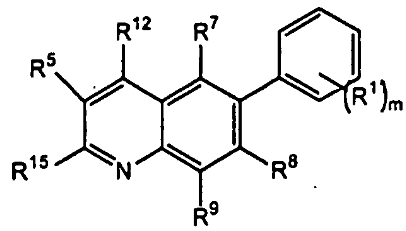
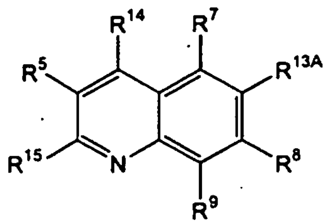


(V)

OR



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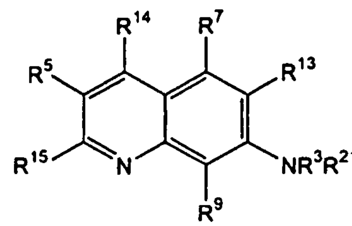
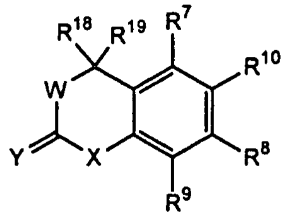


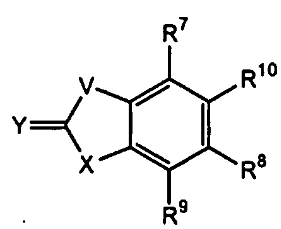
(VI)

OR



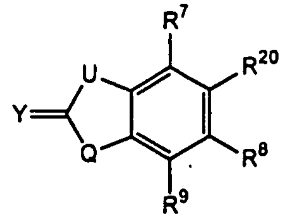
(VII)

OR



(VIII)

OR



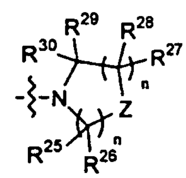
(IX)

wherein:

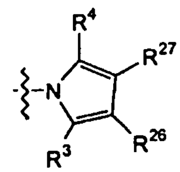
R^1 and R^2 are each independently selected from the group of COR^3, CSR^3, SO_2R^3, NO, NR^3R^4, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_2-C_8 haloalkynyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl, C_2-C_8 heteroalkynyl, $(CH_2)_nR^{3A}$, aryl, and heteroaryl, wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, aryl, and heteroaryl are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, CN, NO_2, SR^3, SOR^3, SO_2R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl; or

R^1 and R^2 taken together form a three- to nine-membered alkyl, alkenyl, heteroalkyl, or heteroalkenyl ring, wherein the alkyl, alkenyl, heteroalkyl, or heteroalkenyl ring are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl; or

R^1 and R^2 are taken together to form one of:



or



R^3 and R^4 are each independently selected from the group of hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, heteroaryl, and aryl, wherein the alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, heteroaryl, and aryl are optionally substituted with halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^{3A} is aryl or heteroaryl, wherein the aryl and heteroaryl is optionally substituted with halogen, CN, NO_2, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^5 is selected from the group of hydrogen, F, Cl, Br, I, OR^3, SR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

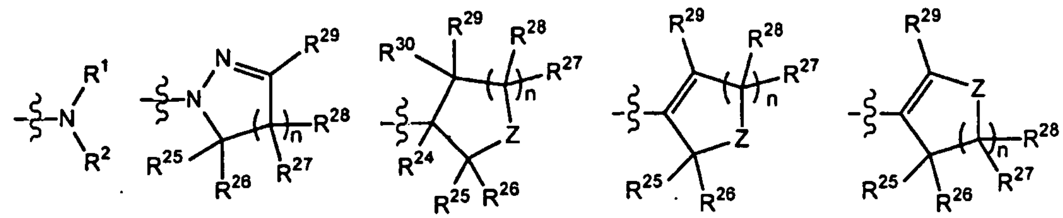
R^6 is selected from the group of F, Cl, Br, I, CH_3, CF_3, CHF_2, CFH_2, CN, CF_2Cl, CF_2OR^3, OR^3, SR^3, SOR^3, SO_2R^3, CO_2R^3, NR^3R^4, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-

C_4 haloalkyl, C_2-C_4 haloalkenyl, C_2-C_4 haloalkynyl, C_1-C_4 heteroalkyl, C_2-C_4 heteroalkenyl, and C_2-C_4 heteroalkynyl, wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl are optionally substituted with F, Cl, Br, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^7 and R^8 are each independently selected from the group of hydrogen, F, Cl, Br, I, CN, OR^3, NR^3R^4, $NR^3CR^3R^4CONR^3R^4$, $C_n(R^3)_{2n}OR^3$, SR^3, SOR^3, SO_2R^3, NR^3COR^4, C_1-C_8 alkyl, C_1-C_8 haloalkyl, and C_1-C_8 heteroalkyl;

R^9 is selected from the group of hydrogen, F, Br, Cl, I, OR^3, NR^3R^4, SR^3, SOR^3, SO_2R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 heteroalkyl;

R^{10} is selected from the group of :



R^{11} is selected from the group of F, Br, Cl, I, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, NO_2, CN, CF_3, OR^3, NR^3R^4, SR^3, SOR^3, and SO_2R^3;

R^{12} is selected from the group of F, Br, Cl, I, CN, OR^3, SR^3, SOR^3, SO_2R^3, NR^3R^4, and C_1-C_4 haloalkyl;

R^{13} is selected from the group of hydrogen, F, Cl, Br, I, CN, OR^3, NR^3R^4, COR^3, CO_2R^3, SR^3, SOR^3, SO_2R^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_2-C_8 haloalkynyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl, C_2-C_8 heteroalkynyl, and $(CH_2)_nR^{3A}$, wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl and heteroalkynyl are optionally substituted with F, Cl, Br, I, CN, NO_2, NR^3R^4, SR^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^{13A} is NHR^1or heteroaryl, wherein the heteroaryl is optionally substituted with F, Cl, Br, I, CN, NO_2, NR^3R^4, SR^3, SOR^3, SO_2R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^{14} is selected from the group of F, Br, Cl, I, CF_3, CHF_2, CH_2F, CF_2Cl, and CF_2OR^3;

R^{15} is selected from the group of F, Br, Cl, I, CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, OR^{16}, $NR^{16}R^4$, SR^{16}, CH_2R^{16}, COR^3, CO_2R^3, $CONR^3R^4$, SOR^3, and SO_2R^3;

R^{16} is selected from the group of hydrogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, CH_2R^{3A}, aryl, heteroaryl, COR^{17}, CO_2R^{17}, and $CONR^{17}R^{17}$;

R^{17} is selected from the group of hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 heteroalkyl;

R^{18} and R^{19} are each independently selected from the group of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 heteroalkyl; or

R^{18} and R^{19} taken together form a three- to seven-membered ring;

R^{20} is aryl or heteroaryl, wherein the aryl or heteroaryl are optionally substituted with F, Cl, Br, CN, OR^3, SR^3, SOR^3, SO_2R^3, NO_2, NR^3R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^{21} is selected from the group of $CR^3R^4CONR^3R^4$, $C_n(R^3)_{2n}OR^3$, SOR^3, SO_2R^3, C_2-C_8 alkyl, C_2-C_8 haloalkyl, and C_2-C_8 heteroalkyl;

R^{22} and R^{23} are each independently selected from the group of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 heteroalkyl; or

R^{22} and R^{23} are taken together to form a three- to seven-membered ring;

R^{24} is hydrogen or OR^3;

R^{25} through R^{30} are each independently selected from the group of hydrogen, F, Cl, Br, I, OR^3, NR^3R^4, SR^3, SOR^3, SO_2R^3, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkynyl and C_2-C_6 alkenyl, wherein the alkyl, haloalkyl, heteroalkyl, alkynyl, and alkenyl are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, aryl or heteroaryl, and wherein the aryl and heteroaryl are optionally substituted with F, Cl, Br, I, CN, NO_2, OH, OCH_3, CF_3 or C_1-C_6 alkyl; or

Any two of R^{25} R^{26}, R^{27}, R^{28}, R^{29} and R^{30} taken together form a three to seven-membered alkyl or alkenyl or heteroalkyl ring; or

any four of R^{25}, R^{26}, R^{27}, R^{28}, R^{29} and R^{30} taken together form a fused aromatic ring;

Q is O or S;

U is selected from the group of V, $OCR^{22}R^{23}$, $SCR^{22}R^{23}$, $NR^3CR^{22}R^{23}$, $CR^3R^4CR^{22}R^{23}$;

V is selected from the group of O, NR^3, $CR^{22}R^{23}$, CR^3R^4O, and CR^3R^4S;

W is selected from the group of O, S, NR^3, and CR^3R^4;

X is selected from the group of O, S and NR^{16};

Y is selected from the group of O, S, NR^3, NOR^3 and CR^3R^4;

Z is selected from the group of O, S, NR^3, C=O, and $CR^{25}R^{26}$; or

Z is two hydrogens;

n is 1, 2 or 3; and

m is 1 to 5,

and pharmaceutically acceptable slats thereof.

2. A compound of claim 1, wherein:

R^3 and R^4 are each independently hydrogen or optionally substituted C_1–C_6 alkyl;

R^{3A} is optionally substituted aryl or heteroaryl;

R^5 is selected from the group of hydrogen, halogen and optionally substituted C_1–C_6 alkyl;

R^7 and R^8 are each independently hydrogen or halogen; and

R^9 is hydrogen or halogen.

3. A compound of claim 2, wherein:

R^{11} is selected form the group of halogen, CN, $N0_2$ and optionally substituted C_1 - C_6 haloalkyl;

R^{12} is halogen or optionally substituted haloalkyl;

R^{13} is selected from the group of hydrogen, halogen, C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl, wherein said C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl are optionally substituted;

R^{15} is halogen or OR^{16}; and

R^{18} and R^{19} are each independently optionally substituted C_1 - C_6 alkyl; or

R^{18} and R^{19} taken together form a five- to six-membered ring.

4. A compound of claim 3, wherein:

R^{22} and R^{23} are each independently hydrogen or optionally substituted C_1 - C_6 alkyl; or

R^{22} and R^{23} taken together form a three- to seven-membered ring;

R^{25} through R^{30} are each independently hydrogen, C_1 - C_6 alkyl, or C_1 - C_6 haloalkyl, wherein said C_1 - C_6 alkyl and C_1 - C_6 haloalkyl are optionally substituted.

Y is selected from the group of O, S, and NOR^3; and
m is 1 to 3.

5. A compound of claim 1, wherein:

R^1 and R^2 are each independently selected from the group of COR^3, CSR^3, SO_2R^3, NO, NR^3R^4, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_2-C_8 haloalkynyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl, C_2-C_8 heteroalkynyl, $(CH_2)_nR^{3A}$, aryl, and heteroaryl, wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, aryl, and heteroaryl are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, CN, NO_2, SR^3, SOR^3, SO_2R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^3 and R^4 are each independently hydrogen or optionally substituted C_1–C_6 alkyl;

R^{3A} is optionally substituted aryl or heteroaryl;

R^5 is selected from the group of hydrogen, halogen and optionally substituted C_1–C_6 alkyl;

R^7 and R^8 are each independently hydrogen or halogen;

R^9 is hydrogen or halogen.

R^{11} is selected form the group of halogen, CN, $N0_2$ and optionally substituted C_1 - C_6 haloalkyl;

R^{12} is halogen or optionally substituted haloalkyl;

R^{13} is selected from the group of hydrogen, halogen, C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl, wherein said C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl are optionally substituted;

R^{15} is halogen or OR^{16};

R^{18} and R^{19} are each independently optionally substituted C_1 - C_6 alkyl; or

R^{18} and R^{19} taken together form a five- to six-membered ring;

R^{22} and R^{23} are each independently hydrogen or optionally substituted C_1 - C_6 alkyl; or

R^{22} and R^{23} together form a three- to seven-membered ring;

R^{25} through R^{30} are each independently hydrogen, C_1 - C_6 alkyl, or C_1 - C_6 haloalkyl, wherein said C_1 - C_6 alkyl and C_1 - C_6 haloalkyl are optionally substituted;

Y is selected from the group of O, S, and NOR^3; and

m is 1 to 3.

6. A compound of claim 1, wherein:

R^1 and R^2 taken together form a three- to nine-membered alkyl, alkenyl, heteroalkyl, or heteroalkenyl ring, wherein the alkyl, alkenyl, heteroalkyl, or heteroalkenyl ring are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^3 and R^4 are each independently hydrogen or optionally substituted C_1–C_6 alkyl;

R^{3A} is optionally substituted aryl or heteroaryl;

R^5 is selected from the group of hydrogen, halogen and optionally substituted C_1–C_6 alkyl;

R^7 and R^8 are each independently hydrogen or halogen;

R^9 is hydrogen or halogen;

R^{11} is selected form the group of halogen, CN, $N0_2$ and optionally substituted C_1 - C_6 haloalkyl;

R^{12} is halogen or optionally substituted haloalkyl;

R^{13} is selected from the group of hydrogen, halogen, C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl, wherein said C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl are optionally substituted;

R^{15} is halogen or OR^{16};

R^{18} and R^{19} are each independently optionally substituted C_1 - C_6 alkyl; or

R^{18} and R^{19} taken together form a five- to six-membered ring;

R^{22} and R^{23} are each independently hydrogen or optionally substituted C_1 - C_6 alkyl; or

R^{22} and R^{23} together form a three- to seven-membered ring;

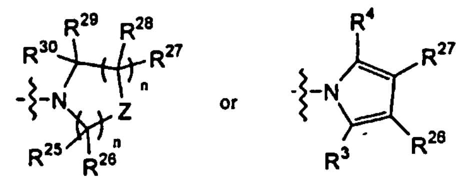
R^{25} through R^{30} are each independently hydrogen, C_1 - C_6 alkyl, or C_1 - C_6 haloalkyl, wherein said C_1 - C_6 alkyl and C_1 - C_6 haloalkyl are optionally substituted;

Y is selected from the group of O, S, and NOR^3; and

m is 1 to 3.

7. A compound of claim 1, wherein:

R^1 and R^2 taken together form one of:



R^3 and R^4 are each independently hydrogen or optionally substituted C_1–C_6 alkyl;

R^{3A} is optionally substituted aryl or heteroaryl;

R^5 is selected from the group of hydrogen, halogen and optionally substituted C_1–C_6 alkyl;

R^7 and R^8 are each independently hydrogen or halogen;

R^9 is hydrogen or halogen;

R^{11} is selected form the group of halogen, CN, $N0_2$ and optionally substituted C_1 - C_6 haloalkyl;

R^{12} is halogen or optionally substituted haloalkyl;

R^{13} is selected from the group of hydrogen, halogen, C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl, wherein said C_1 - C_6 alkyl and C_1 - C_6 heteroalkyl are optionally substituted;

R^{15} is halogen or OR^{16};

R^{18} and R^{19} are each independently optionally substituted C_1 - C_6 alkyl; or

R^{18} and R^{19} taken together form a five- to six-membered ring;

R^{22} and R^{23} are each independently hydrogen or optionally substituted C_1 - C_6 alkyl; or

R^{22} and R^{23} together form a three- to seven-membered ring;

R^{25} through R^{30} are each independently hydrogen, C_1 - C_6 alkyl, or C_1 - C_6 haloalkyl, wherein said C_1 - C_6 alkyl and C_1 - C_6 haloalkyl are optionally substituted;

Y is selected from the group of O, S, and NOR^3; and

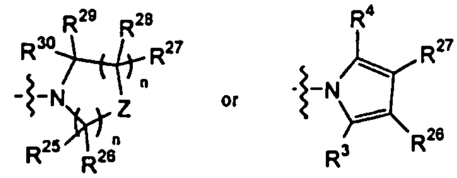
m is 1 to 3.

8. A compound of claim 1, wherein:

R^1 and R^2 are each independently selected from the group of COR^3, CSR^3, SO_2R^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl,

CH_2R^{3A}, aryl and heteroaryl, wherein the aryl or heteroaryl are optionally substituted with F, Cl, Br, CN, NO_2, OR^3, NR^3R^4, SR^3, COMe, $COCF_3$, C_1-C_4 alkyl, or C_1-C_4 haloalkyl; or

R^1 and R^2 are taken together to form one of:



R^3 and R^4 are each independently selected from the group of hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_1-C_8 haloalkyl, and C_1-C_8 heteroalkyl;

R^{3A} is heteroaryl or aryl, wherein the heteroaryl and aryl are optionally substituted with F, Cl, Br, CN, OMe, SMe, C_1-C_4 alkyl, or C_1-C_4 haloalkyl;

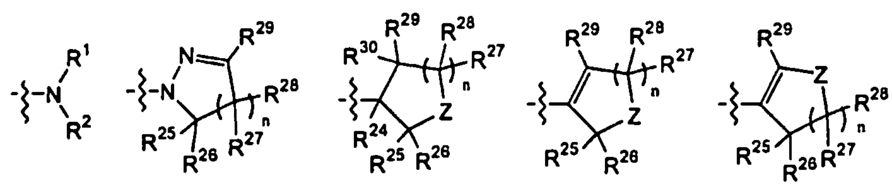
R^5 is selected from the group of hydrogen, F, Cl, Br, OH, OMe, C_1-C_4 alkyl, and C_1-C_4 haloalkyl;

R^6 is selected from the group of F, Cl, Br, CH_3, CF_3, CHF_2, CFH_2, CN, CF_2Cl, CF_2OR^3, OR^3, SR^3, NR^3R^4, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 haloalkyl, C_2-C_4 haloalkenyl, C_1-C_4 heteroalkyl, and C_2-C_4 heteroalkenyl;

R^7 and R^8 are each independently selected from the group of hydrogen, F, Cl, Br, OR^3, NR^3R^4, SR^3, C_1-C_8 alkyl, C_1-C_8 haloalkyl, and C_1-C_8 heteroalkyl;

R^9 is selected from the group of hydrogen, F, Br, Cl, OR^3, NR^3R^4, SR^3, C_1-C_4 alkyl, and C_1-C_4 haloalkyl;

R^{10} is selected from the group of :



R^{11} is selected from the group of F, Br, Cl, I, C_1-C_6 alkyl, C_1-C_6 haloalkyl, NO_2, CN, CF_3, OH, OMe, NR^3R^4, and SR^3;

R^{12} is selected from the group of F, Br, Cl, and C_1-C_4 haloalkyl;

R^{13} is selected from the group of hydrogen, F, Cl, Br, I, CN, OR^3, NR^3R^4, SR^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_2-C_8 haloalkynyl, C_1-C_8 heteroalkyl, and CH_2R^{3A};

R^{13A} is NHR^1or heteroaryl, wherein the heteroaryl is optionally substituted with F, Cl, Br, CN, NMe_2, NO_2, CF_3, Me, or OMe;

R^{14} is selected from the group of F, Br, Cl, CF_3, CHF_2, CH_2F, CF_2Cl, or CF_2OMe;

R^{15} is selected from the group of F, Br, Cl, CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, OR^{16}, $NR^{16}R^4$, and SR^{16};

R^{16} is selected from the group of hydrogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, COR^{17}, CO_2R^{17}, and $CONR^{17}R^{17}$;

R^{17} is selected from the group of C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 heteroalkyl;

R^{18} and R^{19} are each independently selected from the group of C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 heteroalkyl; or

R^{18} and R^{19} are taken together to form a four- to seven-membered ring;

R^{20} is aryl or heteroaryl, optionally substituted with F, Cl, Br, CN, NO_2, CF_3, or C_1-C_4 alkyl;

R^{21} is selected from the group of C_2-C_8 alkyl, C_2-C_8 haloalkyl, or C_2-C_8 heteroalkyl;

R^{22} and R^{23} are each independently selected from the group of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 heteroalkyl; or

R^{22} and R^{23} are taken together to form a three- to seven-membered ring;

R^{24} is hydrogen or OR^3;

R^{25} through R^{30} are each independently selected from the group of hydrogen, F, Cl, Br, OR^3, NR^3R^4, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl and C_2-C_6 alkenyl, wherein the alkyl, haloalkyl, heteroalkyl, and alkenyl are optionally substituted with F, Cl, Br, OR^3, NR^3R^4, aryl or heteroaryl, and wherein the aryl and heteroaryl are optionally substituted with F, Cl, Br, CN, NO_2, OH, OCH_3, CF_3 or C_1-C_6 alkyl;

Any two of R^{25}, R^{26}, R^{27}, R^{28}, R^{29} and R^{30} taken together form a three to seven-membered alkyl or alkenyl or heteroalkyl ring; or

Any four of R^{25}, R^{26}, R^{27}, R^{28}, R^{29} and R^{30} taken together form a fused aromatic ring;

Q is O;

U is selected from the group of V, $OCR^{22}R^{23}$, $NR^3CR^{22}R^{23}$, $CR^3R^4CR^{22}R^{23}$;

V is selected from the group of $CR^{22}R^{23}$, CR^3R^4O, and CR^3R^4S;

W is selected from the group of O, NR^3, and CR^3R^4;

X is S or NR^{16};

Y is selected from the group of O, S, NR^3, and NOR^3;

Z is selected from the group of O, S, NR^3, and $CR^{25}R^{26}$, or

Z is two hydrogens;

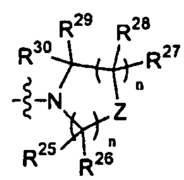
n is 1 or 2; and

m is 1 to 4.

9. A compound of claim 1, wherein said compound is represented by any one of formula I through formula VIII:

R^1 and R^2 are each independently selected from the group of COR^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_1-C_8 heteroalkyl, CH_2R^{3A}, aryl, and heteroaryl, wherein the aryl and heteroaryl are optionally substituted with F, Cl, Br, OH, OMe, SH, OMe, SMe, CN, NO_2, CF_3, Me, COMe, or $COCF_3$; or

R^1 and R^2 are taken together to form:



R^3 and R^4 are each independently selected from the group of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

R^{3A} is heteroaryl or aryl, wherein the heteroaryl and aryl are optionally substituted with F, Cl, Br, CN, OMe, C_1-C_4 alkyl, or C_1-C_4 haloalkyl;

R^5 is selected from the group of hydrogen, F, Cl, OH, OMe, C_1-C_4 alkyl, and CF_3;

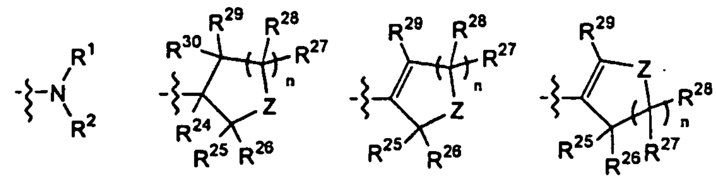
R^6 is selected from the group of F, Cl, Br, C_1-C_4 alkyl, CF_3, CHF_2, CFH_2, CN, CF_2Cl, CF_2OMe, and OMe;

R^7 is selected from the group of hydrogen, F, Cl, Me, OMe, and CF_3;

R^8 is selected from the group of hydrogen, F, Cl, Br, OR^3, NR^3R^4, C_1-C_6 alkyl, C_1-C_6 haloalkyl, and C_1-C_6 heteroalkyl;

R^9 is selected from the group of hydrogen, F, Cl, OH, Me, OMe, and CF_3;

R^{10} is selected from the group of:



R^{11} is selected from the group of F, Br, Cl, C_1-C_6 alkyl, NO_2, CN, CF_3, OH, and OMe;

R^{12} is selected from the group of F, Cl, CF_3, CF_2H, and CFH_2;

R^{13} is selected from the group of hydrogen, F, Cl, Br, OR^3, SR^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, and C_1-C_8 haloalkyl;

R^{13A} is NHR^1;

R^{14} is selected from the group of F, Cl, CF_3, CHF_2, CH_2F, and CF_2Cl;

R^{15} is selected from the group of F, Cl, CN, CF_3, OR^{16}, and SR^{16};

R^{16} is selected from the group of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, COR^{17}, CO_2R^{17}, and $CONR^{17}R^{17}$;

R^{17} is selected from the group of C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 heteroalkyl;

R^{18} and R^{19} are each independently selected from the group of C_1-C_6 alkyl, C_1-C_6 haloalkyl; or

R^{18} and R^{19} taken together form a five- to six-membered ring;

R^{21} is C_2-C_8 alkyl or C_2-C_8 haloalkyl;

R^{22} and R^{23} are each independently selected from the group of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl; or

R^{22} and R^{23} taken together form a four- to six-membered ring;

R^{24} is hydrogen or OH;

R^{25} through R^{30} are each independently selected from the group of hydrogen, F, Cl, OH, OMe, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl and C_2-C_6 alkenyl; or

Any two of R^{25} R^{26}, R^{27}, R^{28}, R^{29} and R^{30} taken together form a four to six-membered alkyl or alkenyl ring; or

Any four of R^{25} R^{26}, R^{27}, R^{28}, R^{29} and R^{30} taken together form a fused aromatic ring;

V is selected from the group of $CR^{22}R^{23}$, CR^3R^4O, and CR^3R^4S;

W is O or CR^3R^4;

X is O or NR^{16};

Y is selected from the group of O, S, and NOR^3;

Z is O or $CR^{25}R^{26}$; or

Z is two hydrogens;

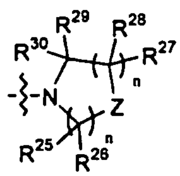
n is 1 or 2; and

m is 1 to 3.

10. A compound of claim 1, wherein said compound is represented by any one of formula I, III, IV and VI – VIII, and wherein:

R^1 and R^2 are each independently selected from the group of C_1-C_8 alkyl, C_2-C_8 alkenyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, and CH_2R^{3A}; or

R^1 and R^2 are taken together to form:



R^3 and R^4 are each independently selected from the group of hydrogen, C_1-C_6 alkyl, and C_1-C_6 haloalkyl;

R^{3A} is heteroaryl or aryl, wherein the heteroaryl and aryl are optionally substituted with F, Cl, Br, CN, CF_3, OMe, or C_1-C_4 alkyl;

R^5 is selected from the group of hydrogen, F, Cl, OMe, and Me;

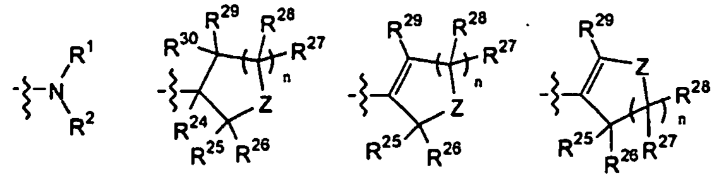
R^6 is selected from the group of F, Cl, C_1-C_4 alkyl, CF_3, CHF_2, CFH_2, CF_2Cl, CF_2OMe, and OMe;

R^7 is selected from the group of hydrogen, F, Cl, Me, OMe;

R^8 is selected from the group of hydrogen, F, Cl, Br, OR^3, NR^3R^4, C_1-C_6 alkyl, C_1-C_6 haloalkyl;

R^9 is selected from the group of hydrogen, F, Cl, Me, OMe, CF_3;

R^{10} is selected from the group of:



R^{13} is selected from the group of hydrogen, F, Cl, Br, C_1-C_4 alkyl, C_2-C_4 alkenyl, and C_1-C_8 haloalkyl;

R^{13A} is NHR^1;

R^{14} is selected from the group of Cl, CF_3, CHF_2, CH_2F, and CF_2Cl;

R^{15} is selected from the group of Cl, OR^{16} and SR^{16};

R^{16} is selected from the group of hydrogen, C_1-C_6 alkyl, COR^{17}, CO_2R^{17}, and $CONR^{17}R^{17}$;

R^{17} is selected from the group of C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 heteroalkyl;

R^{18} and R^{19} are each independently C_1-C_4 alkyl or C_1-C_4 haloalkyl; or

R^{18} and R^{19} are taken together to form a five- to six-membered ring;

R^{21} is selected from the group of C_2-C_8 alkyl, C_2-C_8 haloalkyl, and C_2-C_8 heteroalkyl;

R^{24} is hydrogen or OH;

R^{25} through R^{30} are each independently selected from the group of hydrogen, F, Cl, OH, OMe, C_1-C_4 alkyl, and C_1-C_4 haloalkyl;

W is O;

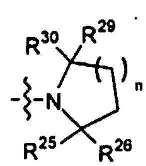
X is NR^{16};

Y is O or S;

Z is two hydrogens; and

n is 1 or 2.

11. A compound of claim 1, wherein R^{10} is represented by the formula:

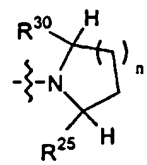


R^{25}, R^{26}, R^{29}, R^{30} are each independently selected from the group of hydrogen, F, Cl, Br, I, OR^3, NR^3R^4, SR^3, SOR^3, SO_2R^3, COR^3, CO_2R^3, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkynyl and C_2-C_6 alkenyl, wherein the alkyl, haloalkyl, heteroalkyl, alkynyl, and alkenyl are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl, aryl or heteroaryl, and wherein the aryl and heteroaryl are optionally substituted with F, Cl, Br, I, CN, NO_2, OH, OCH_3, CF_3 or C_1-C_6 alkyl;

R^3 and R^4 are each independently selected from the group of hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, heteroaryl, and aryl, wherein the alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, heteroaryl, and aryl are optionally substituted with halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl; and

n is 1, 2, 3 or 4.

12. A compound of claim 1, wherein R^{10} is represented by the formula:



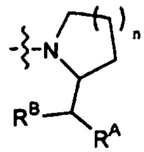
wherein:

R^{25}, R^{30} are each independently selected from the group of hydrogen, F, Cl, Br, I, OR^3, NR^3R^4, SR^3, SOR^3, SO_2R^3, COR^3, CO_2R^3, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkynyl and C_2-C_6 alkenyl, wherein the alkyl, haloalkyl, heteroalkyl, alkynyl, and alkenyl are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, aryl or heteroaryl, and wherein the aryl and heteroaryl are optionally substituted with F, Cl, Br, I, CN, NO_2, OH, OCH_3, CF_3 or C_1-C_6 alkyl;

R^3 and R^4 are each independently selected from the group of hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, heteroaryl and aryl, wherein the alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, heteroaryl, and aryl are optionally substituted with halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl; and

n is 1, 2, 3 or 4.

13. A compound of claim 1, wherein R^{10} is represented by the formula:



wherein:

R^A is selected from the group of hydrogen, OR^C, O_2CR^C, $(CH_2)_nOR^C$, NHR^C, $NHCOR^C$, F, Cl, Br, I, CN, SCN, and SCH_3;

R^B is selected from the group of hydrogen, F, Cl, Br, I, CHF_2, CF_3, C_1-C_6 alkyl, aryl, and heteroaryl, wherein the alkyl, aryl and heteroaryl are optionally substituted with F, Cl, Br, I, CN, NO_2, OH, OCH_3, CF_3, or C_1-C_6 alkyl;

R^C is selected from the group of hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, and $(CH_2)_nR^D$;

R^D is aryl or heteroaryl, optionally substituted with F, Cl, Br, I, CN, NO_2, OH, OCH_3, CF_3, or C_1-C_6 alkyl; and

n is 1, 2, or 3.

14. A compound according to claim 1, wherein the compound is an androgen receptor modulator.

15. A compound according to claim 14, wherein the compound is an androgen receptor antagonist.

16. A compound according to claim 14, wherein the compound is an androgen receptor agonist.

17. A compound according to claim 14, wherein the compound is an androgen receptor partial agonist.

18. A compound according to claim 1, wherein the compound is a progesterone receptor modulator.

19. A compound according to claim 18, wherein the compound is a progesterone receptor antagonist

20. A compound according to claim 18, wherein the compound is a progesterone receptor agonist.

21. A compound according to claim 18, wherein the compound is a progesterone receptor partial agonist.

22. A compound according to claim 1, wherein the compound is selected from the group of:

6-Propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **204**);

6-Isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **205**);

6-Isobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **206**);

6-(2,2-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **207**);

6-Cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **208**);

6-(2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **209**);

6-(2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **210**);

6-(2,2-Difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **211**);

6-(2-Chloro-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **212**);

6-Acetylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **213**);

6-Trifluoroacetylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **214**);

6-Benzoylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **215**);

6-Dimethylacetylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **216**);

6-Dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **217**);

6-Diethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **218**);

6-Dipropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **219**);

6-Dibutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **220**);

6-Diisobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **221**);

6-(bis-Cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **222**);

6-(bis-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **223**);

6-(bis-2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **224**);

6-(bis-2-Chloro-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **225**);

6-(bis-2-Bromoethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **226**);

6-(N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **227**);

6-(bis-N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **228**);

6-(N-2,2,2-Chlorodifluoroethyl-N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **229**);

6-(bis-N-2,2-Difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **230**);

6-(N-2,2-Dichloroethyl-N-2,2,2-trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **231**);

6-(bis-N-2,2-Dichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **232**);

6-(N-2,2-Dichloroethyl-N-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **233**);

6-(N-2,2-Dichloroethyl-N-2,2,2-chlorodifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **234**);

6-(N-Isopropyl-N-methyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **235**);

6-(N-Methyl-N-cyclopentyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **236**);

6-(N-Methyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **237**);

6-(N-Ethyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **238**);

6-(N-Ethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **239**);

6-(N-Ethyl-N-1-methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **240**);

6-(N-Ethyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **241**);

6-(N-Ethyl-N-2,2-dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **242**);

6-(N-Ethyl-N-cyclopentyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **243**);

6-(N-Ethyl-N-1-acetylethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **244**);

(±)-6-(N-Ethyl-N-1-methyl-2-hydroxypropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **245**);

6-(N-Ethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **246**);

6-(N-Ethyl-N-3-furylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **247**);

(±)-6-(N-Ethyl-N-2,2-dimethoxyisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **248**);

6-(N-Isopropyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **249**);

6-(N-2-Hydroxyethyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **250**);

(±)-6-(N-Propyl-N-1-methylbutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **251**);

(±)-6-(N-Propyl-N-1,2-dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **252**);

6-(N-Propyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **253**);

6-(N-Propyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **254**);

(±)-6-(N-Propyl-N-1-methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **255**);

6-(N-2-Hydroxyethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **256**);

6-(N-Isopropyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **257**);

6-(N-Methyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **258**);

6-(N-2,2,2-trifluoroethyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **259**);

6-(N-2,2,2-trifluoroethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **260**);

6-(N-2,2,2-Trifluoroethyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **261**);

(±)-6-(N-2,2,2-Trifluoroethyl-N-1-methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **262**);

(±)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **263**);

(+)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **264**);

(-)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **265**);

6-(N-2,2,2-Trifluoroethyl-N-3-furfuryl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **266**);

6-(N-2,2,2-Trifluoroethyl-N-3-thiophenemethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **267**);

6-(N-2,2,2-Trifluoroethyl-N-3,3-dimethylbutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **268**);

6-(N-2,2,2-Trifluoroethyl-N-2-thiophenemethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **269**);

6-(N-2,2,2-Trifluoroethyl-N-2-furfuryl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **270**);

6-(N-Butyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **271**);

6-(bis-N,N-Benzyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **272**);

6-(N-2,2,2-Trifluoroethyl-N-cyclobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **273**);

6-(N-2,2,2-Trifluoroethyl-N-2,2-dichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **274**);

6-(N-2,2,2-Trifluoroethyl-N-2-chloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **275**);

6-(N-Benzyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **276**);

6-(N-4-Fluorobenzyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **277**);

6-(N-Propyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **278**);

6-(N-2,2,3,3,3-Pentafluoropropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **279**);

6-Diallylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **280**);

6-(N-Isobutyl-N-allyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **281**);

6-(N-Isopropyl-N-allyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **282**);

6-(N-Allyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **283**);

6-Allylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **284**);

6-(N-Allyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **285**);

6-(N-Allyl-N-2,2,2-trifluoroacetyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **286**);

6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroacetyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **287**);

6-(N-Allyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **288**);

(±)-6-(N-2-Hydroxyisopropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **289**);

(±)-6-(N-Isobutyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **290**);

6-(N-2,2-Difluoroethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **291**);

6-(N-2,2-Dimethylpropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **292**);

6-(N-2,2-Difluoro-2-chloroethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **293**);

6-(N-2,2-Difluoro-2-chloroethyl-N-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **294**);

6-(N-2,2,2-Trifluoroethyl-N-methylsufonyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **295**);

1-Methyl-6-(N-propyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **296**);

1-Methyl-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **297**);

1-Ethyl-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **298**);

6-(N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **299**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **300**);

(±)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **301**);

(+)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **302**);

(-)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **303**);

6-Methoxythiocarbonylmercapto-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **304**);

6-(1,1-Dimethyl-2-propynyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **306**);

6-*tert*-Butylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **307**);

6- *tert*-Butylamino-2-isopropyloxy-4-trifluoromethylquinolines (Compound **310**);

6-(1-Piperdinyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **311**);

6-(1-Pyrrolidinyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **312**);

6-(1-Morpholino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **313**);

(±)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **314**);

(+)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **315**);

(-)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **316**);

6-(N-phenylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **317**);

6-(N-phenyl-N-ethylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **319**);

6-(N-phenyl-N-ethylamino)-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **320**);

6-(N-phenyl-N-2,2,2-trifluoroethylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **321**);

(±)-6-(3-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **322**);

6-(4-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **323**);

6-(*cis*-3,5-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **324**);

6-(2,6-*cis*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **325**);

6-(2,6-*trans*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **326**);

(±)-6-(2-Methyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **327**);

6-(2,5-*cis*-Dimethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **328**);

(±)-6-(2,5-*trans*-Dimethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **329**);

6-(1-Azepano)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **330**);

(±)-6-(2-Hydroxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)--quinolinone (Compound **331**);

6-(2,5-cis-Dimethyl-1-pyrrolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **332**);

(±)-6-(2-Propyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **333**);

(±)-6-(2-Methoxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **334**);

(±)-6-(2-Ethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **335**);

6-(1-Cycloheptylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **336**);

(±)-6-(2-Ethoxycarbonyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **337**);

(±)-6-(2-Isopropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **338**);

(±)-6-(2-Hydroxycarbonyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **339**);

6-(3,5-*cis*-Dimethyl-1-piperazino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **340**);

(±)-6-(2-Benzyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **341**);

(±)-6-(5-Methyl-2-oxo-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **342**);

(±)-6-(2-(2-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **343**);

(±)-6-(3-Hydroxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **344**);

(±)-6-(3-Acetyloxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **345**);

(±)-6-(3-Hydroxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **346**);

6-(1-Indolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **347**);

6-(1-Tetrahydroquinolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **348**);

6-(2-Tetrahydroisoquinolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **349**);

(±)-6-(1,3,3-Trimethyl-6-azabicyclo[3.2.1]octanyl-6-)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **350**)

(±)-6-(2-Trifluoromethyl-5-*cis*-methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **351**);

(±)-6-(2-Trifluoromethyl-5-*trans*-methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **352**);

6-N-(1-Hydroxyisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **353**);

(±)-6-(2-Trifluoromethyl-5-cis-ethyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **354**);

(±)-6-(2-Trifluoromethyl-5-trans-ethyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **355**);

(±)-6-(5-Methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **356**);

6-(2,5-Dimethyl-1-pyrrolyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **357**);

6-(N-2,2,2-Trifluoroethyl-N-3,3,3-trifluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **358**);

6-(N-3,3,3-Trifluoropropyl)amino-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **360**);

6-bis-N,N-Thiomethoxymethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **361**);

6-bis-N,N-Thiomethoxymethylamino-4-trifluoromethyl-2-thiomethoxymethyloxyquinoline (Compound **362**);

(±)-6-(2,5-*trans*-Diethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **363**);

6-(2,5-*cis*-Diethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **364**);

(±)-6-(2,5-*trans*-Dipropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **365**);

6-(2,5-*cis*-Dipropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **366**);

6-(2,5-Dipropyl-1-pyrrolo)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **367**);

6-(2,5-*cis*-Dibutyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **368**);

(±)-6-(2,5-*trans*-Dibutyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **369**);

6-(2,6-*cis*- Diethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **370**);

(±)-6-(2,6-*trans*-Diethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **371**);

6-(2,6-*cis*- Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **372**);

(±)-6-(2,6-*trans*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **373**);

6-(N-Propyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **374**);

6-(bis-2,2,2-Trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **377**);

6-(2,5-Dimethyl-1-pyrrolyl)-4-methyl-2(1*H*)-quinolinone (Compound **378**);

(±)-6-(2,5-*trans*-dimethyl-1-pyrrolidino)-4-methyl-2(1*H*)-quinolinone (Compound **379**);

6-(2,5-*cis*-dimethyl-1-pyrrolidino)-4-methyl-2(1*H*)-quinolinone (Compound **380**);

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **381**);

6-(N-2,2,2-Chlorodifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **382**);

6-(bis-N,N-2,2,2-Chlorodifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **383**);

6-(N-2,2,2-Chlorodifluoroethyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **384**);

6-N-Ethylamino-4-methyl-2(1*H*)-quinolinone (Compound **385**);

6-(N-Ethyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **386**);

6-N,N-Diethylamino-4-methyl-2(1*H*)-quinolinone (Compound **387**);

6-(bis-2,2,2-trifluoroethyl)amino-4-ethyl-2(1*H*)-quinolinone (Compound **388**);

6-(bis-2,2,2-trifluoroethyl)amino-4-isopropyl-2(1*H*)-quinolinone (Compound **391**);

7-Fluoro-6-(bis-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **393**);

8-Fluoro-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **397**);

8-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 316); 6-Amino-8-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **399**);

8-Fluoro-6-(N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **400**);

8-Fluoro-6-(N-2,2,2-trifluoroethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **401**);

3-Fluoro-6-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **403**);

3-Fluoro-6-(bis-2,2,2-trifluorofluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **404**);

6-(bis-Isobutylamino)-4-methyl-2(1*H*)-quinolinone (Compound **405**);

3-Fluoro-6-(N-methyl-N-2,2,2-trifluorofluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **406**);

7-Bromo-6-isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **407**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-hydroxy-2(1*H*)-quinolinone (Compound **409**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-methoxy-2(1*H*)-quinolinone (Compound **411**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-difluoromethyl-2(1*H*)-quinolinone (Compound **413**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **415**);

4-Chloro-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **417**);

(*R*)-6-(2-Hydroxymethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **421**);

(*R*)-6-(2-Methoxycarbonyl-1-pyrrolidino)-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **422**);

(*R*)-6-(2-Methoxymethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **423**);

(±)-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **424**);

(±)-6-(2-Cyanothiomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **425**);

(±)-6-(2-Thiomethoxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **426**);

(±)-6-(2-Cyanomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **427**);

(±)-6-(2-Bromomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **428**);

(±)-6-(2-Iodomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **429**);

(+)*R*-6-(2-Iodomethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **430**);

(±)-6-(2-Fluoromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **431**);

(+)S-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **432**);

(-)R-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **433**);

(+)*R*-6-(2-Chloromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **434**);

(-)*S*-6-(2-Chloromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **435**);

R-6-(2-Difluoromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **436**);

(±)-6-(2*l*-(1*l*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **437**);

(±)-6-(2*l*-(1*u*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **438**);

(±)-6-(2-Formyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **439**);

(±)-6-(2-Difluoromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **440**);

(±)-6-(2-Aminomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **441**);

(*R*)-6-(2-Vinyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **442**);

(*R*)-6-(2-Formyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **443**);

(±)-6-(2-Vinyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **444**);

(±)-6-(2-Benzyloxyethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **445**);

(±)-6-(2-(2,2-Difluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **446**);

(±)-6-(2-Trifluoroacetamidomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **447**);

(±)-6-(2-(2-Ethoxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **448**);

(±)-6-(2-(4-Trifluoromethyl)benzyloxyethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **449**);

(+)-6-(2*R*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **450**);

(-)6-(2*R*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **451**);

6-(2*S*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **452**);

6-(2*S*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **453**);

(±)-6-(2*l*-(1*l*-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **454**);

(±)-6-(2*l*-(1*u*-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **455**);

(-)-6-(2*S*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **456**);

(+)-6-(2*R*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **457**);

(+)-6-(2*R*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **458**);

(-)-6-(2*S*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **459**);

(±)-6-(2*l*-(1*l*-Acetyloxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **460**);

(±)-6-(2*l*-(1*u*-Acetyloxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **461**);

(±)-6-(2*l*-(1*u*-Methoxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **462**);

(±)-6-(2*l*-(1*l*-Methoxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **463**);

7-Methoxy-6-(N-methyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **464**);

7-Methoxy-6-(N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **467**);

7-Methoxy-6-(N-ethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **468**);

7-Hydroxy-6-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **469**);

6-(N-Cyclopropylmethyl-N-2,2,2-trifluoroethyl)amino-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **470**);

6-(N-Cyclopropylmethyl-N-2,2,2-trifluoroethyl)amino-7-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **471**);

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **472**);

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-7-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **473**);

6-(bis-2,2,2-Trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound **474**);

(±)-3,4-Dihydro-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound **476**);

6-(2,2,2-trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound **477**);

6-(N-Isopropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound **478**);

6-N-Isobutylamino-4-trifluoromethylcoumarin (Compound **479**);

6-N,N-Diethylamino-4-trifluoromethylcoumarin (Compound **480**);

6-N,N-Dipropylamino-4-trifluoromethylcoumarin (Compound **481**);

6-N-Propylamino-4-trifluoromethylcoumarin (Compound **482**);

6-(N-Isobutyl-N-propylamino)-4-trifluoromethylcoumarin (Compound **483**);

6-(N-2,2,2-Trifluoroethyl-N-propylamino)-4-trifluoromethylcoumarin (Compound **484**);

1,4-Dihydro-4,4-dimethyl-6-methylamino-1,3-benzo[d]oxazin-2-one (Compound **485**);

1,4-Dihydro-4,4-dimethyl-6-dimethylamino-1,3-benzo[d]oxazin-2-one (Compound **488**);

1,4-Dihydro-4,4-dimethyl-6-dipropylamino-1,3-benzo[d]oxazin-2-one (Compound **489**);

1,4-Dihydro-4,4-dimethyl-6-(bis-N,N-2,2,2-trifluoroethyl)amino-1,3-benzo[d]oxazin-2-one (Compound **490**);

1,4-Dihydro-4,4-dimethyl-6-(N-2,2,2-trifluoroethyl)amino-1,3-benzo[d]oxazin-2-one (Compound **491**);

(±)-1,4-Dihydro-4-methyl-6-diallylamino-1,3-benzo[d]oxazin-2-one (Compound **492**);

6-Diallylamino-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **497**);

3,4-Dihydro-4,4-dimethyl-6-dipropylamino-2(1*H*)-quinolinone (Compound **498**);

3,4-Dihydro-4,4-dimethyl-6-propylamino-2(1*H*)-quinolinone (Compound **499**);

3,4-Dihydro-4,4-dimethyl-6-(N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **500**);

3,4-Dihydro-4,4-dimethyl-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **501**);

3,4-Dihydro-6-(N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **502**);

3,4-Dihydro-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **505**);

5-(bis-N,N-2,2,2-Trifluoroethyl)amino-3,3-spirocyclohexyl-2-indolone (Compound **506**);

7-(bis-N,N-2,2,2-Trifluoroethyl)amino-1,4-benzoxazin-3(4*H*)-one (Compound **508**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-2,4-dichloroquinoline (Compound **510**);

7-Propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **513**);

7-Isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **514**);

7-(2,2-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **515**);

7-(2-Methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **516**);

7-Benzylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **519**);

7-(2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **520**);

7-Butylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **521**);

7-Ethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **522**);

7-(N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **523**);

7-Cyclohexylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **524**);

7-Cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **525**);

7-Cyclobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **526**);

7-(2-Hydroxy-2-methylpropionyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **527**);

7-(Trifluoroacetamido)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **528**); 1-Methyl-7-methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **529**);

1-Methyl-7-(N-methyl-N-isopropylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **531**);

1-Methyl-7-(2,2,2-trifluoromethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **532**);

3-Fluoro-7-(2,2,2-trifluoromethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **533**);

3-Fluoro-7-isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **535**);

3-Fluoro-7-cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **536**);

3-Fluoro-7-cyclohexylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **537**);

3-Fluoro-7-cyclobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **538**);

3-Fluoro-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **539**);

3-Fluoro-1-methyl-7-(N-methyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **540**);

3-Fluoro-1-methyl-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **541**);

6-Fluoro-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **543**);

6-Fluoro-7-isobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **544**);

6-Fluoro-1-methyl-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **545**);

6-Fluoro-1-methyl-7-(N-methyl-N-propylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **546**);

7-Isobutylamino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **548**);

7-Propylamino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **549**);

7-(1,1-Dimethyl-3-oxobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **550**);

7-(1,1,3-Trimethyl-3-hydroxybutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **551**);

7-(1,1,3-Trimethyl-3-butenylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **552**);

7-(1-Phenylaminocarbonylisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **553**);

7-(2-Hydroxy-1,1-dimethylethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **556**);

7-(N-1-Formylisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **558**);

7-(1,1-Dimethylallyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **559**);

7-(1,1-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **560**);

7-(1-Methyl-1-acetylenylpropyl)amino]-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **561**);

7-(1-Ethyl-1-methylpropyl)amino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **562**);

8-Methyl-7-(3-methyl-2-butenyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **563**);

8-Methyl-7-(3-methylbutyl)amino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **566**);

8-Methyl-7-propylamino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **567**);

8-Methyl-7-isobutylamino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **569**);

7-Amino-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **571**);

7-Isobutylmino-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **574**);

7-(2-Picolylamino)-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **575**);

7-Amino-6-cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **582**);

6-Ethyl-7-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **585**);

6-Isobutyl-7-methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **588**);

7-(1-Morpholino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **589**);

6-(bis-N,N-2,2,2-trifluoroethyl)amino-5-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **600**);

6-(N-2,2,2-Trifluoroethyl)amino-5-propyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **602**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-propyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **604**);

6-(N-2,2,2-Trifluoroethyl)amino-5-ethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **605**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-ethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **607**);

6-(N-2,2,2-Trifluoroethyl)amino-5-(3,3,3-trifluoropropyloxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **608**);

6-(N-2,2,2-Trifluoroethyl)amino-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **610**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **612**);

6-Cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **616**);

6-(1- *trans*-Propenyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **617**);

6-Cyclohexyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **618**);

6-(1-Hydroxy-3,3,5,5-tetramethyl)cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **625**);

6-(3,3,5,5-Tetramethyl)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **626**);

6-(5,5-Dimethycyclopentenyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **627**);

6-(2,2-Dimethycyclopentyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **628**);

6-(1-Hydroxycyclohexyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **629**);

6-Cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **630**);

6-Cyclohexyl-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **631**);

6-Cyclopentenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **632**);

6-Cycloheptenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **633**);

6-Cyclohexenyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **635**);

6-Cyclohexyl-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **636**);

6-Cyclopentyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **638**);

(Z)-6-(1-Propyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **639**);

(E)-6-(1-Propyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **640**);

6-(1-Propyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **641**);

(E)-6-(1-Methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **642**);

(Z)-6-(1-Methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **643**);

(±)-6-(1-Methyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **644**);

(E)-6-(1-Ethyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **645**);

(Z)-6-(1-Ethyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **646**);

6-(1-Ethyl)propyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **647**);

6-(1-Isopropyl-2-methyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **648**);

6-(1-Isopropyl-2-methyl)propyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **649**);

(Z)-6-(1-Isobutyl-3-methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **650**);

(E)-6-(1-Isobutyl-3-methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **651**);

6-(1-Isobutyl-3-methyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **652**);

6-(1-Propyl)butyl-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **653**);

6-(3-Oxo-1-)cyclopentenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **654**);

6-(3-Oxo-1-)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **655**);

6-(3-Oxo-1-)cyclopentenyl-3-methyl-4-difluoromethyl-2(1*H*)-quinolinone (Compound **656**);

6-(3-Oxo-1-)cyclohexenyl-3-mehyl-4-difluoromethyl-2(1*H*)-quinolinone (Compound **657**);

(±)-6-(3-Hydroxy-1-)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **658**);

6-(1-Hydroxy-1,1-diphenyl)methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **659**);

6-(3-hydroxy-3-methyl-1-)butynyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **661**);

6-(1-Hydroxy)cyclopentyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **662**);

6-(1-Cyclopentenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **664**);

6-Cyclopentyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **665**);

6-(1-Hydroxy)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **666**);

6-(1-Cyclohexenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **667**);

6-Cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **668**);

6-(1-Hydroxy)cycloheptyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **669**);

6-(1-Cycloheptenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **670**);

6-(1-Cycloheptyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **671**);

6-(2,6,6-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **672**);

(±)-6-(3,3,5-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **673**);

(±)-6-(3,5,5-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **674**);

(±)-6-(5-Methyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **675**);

(±)-6-(3-Methyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **676**);

(±)-6-(2,6-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **677**);

(±)-6-(2-Bicyclo[2.2.1]heptenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **678**);

(±)-6-(4,5-*trans*-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **679**);

(±)-6-(3,4-*trans*-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **680**);

6-(6,6-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **681**);

6-(5,5-Dimethyl-1-)cyclopentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **682**);

(±)-6-(3,3,5-*cis*-Trimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **683**);

(±)-6-(3,3,5-*trans*-Trimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **684**);

(±)-6-(3-*cis*-Methyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **685**);

(±)-6-(3-*trans*-Methyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **686**);

(±)-6-(2,6-cis,cis-Dimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **687**);

(*E*)-6-(1,4-Dimethyl-1-)pentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **688**);

6-(1-Cyclohexenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **689**);

6-(3-Oxo-1-)cyclopentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **690**);

6-(3-Oxo-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **691**);

(±)-6-(3-Hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **692**);

(±)-6-(3-*cis*-Hydroxy)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **693**);

(±)-6-(3-Butyl-3-hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **694**);

6-(3-Oxo-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **695**);

(±)-6-(3-Hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **697**);

(±)-6-(1-Cyclohexenyl)-1,4-dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **698**);

6-(1-Cyclohexenyl)-1,4-dihydro-4,4,5-trimethyl-1,3-benzo[d]oxazin-2-one (Compound **701**);

6-(1-Cyclohexenyl)-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **705**);

6-Cyclohexyl-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **707**);

(±)-8-Bromo-6-(1-cyclohexenyl)-1,4-dihydro-4-trifluoromethyl-1,3-benzo[d]oxazin-2-one (Compound **708**);

5-(3-Oxo-1-)cyclohexenyl-3,3-dimethyl-2-indolone (Compound **712**);

(±)-5-(3-Hydroxy-1-)cyclohexenyl-3,3-dimethyl-2-indolone (Compound **714**);

(±)-5-(3-Oxocyclohexyl)-3,3-dimethyl-2-indolone (Compound **715**);

5-Cyclohexyl-3,3-spirocyclohexyl-2-indolone (Compound **716**);

5-Cyclopentyl-3,3-spirocyclohexyl-2-indolone (Compound **718**);

6-(1-Hydroxycyclohexyl)-2(3*H*)-benzothiozolone (Compound **719**);

6-Cyclohexenyl-2(3*H*)-benzothiozolone (Compound **720**);

1-Benzyl-6-cyclohexyl-3,4-dihydro-3-methyl-2(1*H*)-quinazolinone (Compound **724**);

6-(2,3-Difluoro)phenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **725**);

4-Trifluoromethyl-6-(3-nitro)phenyl-2(1*H*)-quinolinone (Compound **727**);

4-Trifluoromethyl-6-(3,5-dichloro)phenyl-2(1*H*)-quinolinone (Compound **728**);

4-Trifluoromethyl-6-(3-fluoro-5-N-hydroxyliminomethyl)phenyl-2(1*H*)-quinolinone (Compound **729**);

4-Trifluoromethyl-6-(3-fluoro-5-formylmethylphenyl)-2(1*H*)-quinolinone (Compound **730**);

4-Trifluoromethyl-6-(3-fluoro-5-cyano)phenyl-2(1*H*)-quinolinone (Compound **731**);

4-Trifluoromethyl-6-(3-fluoro-5-chloro)phenyl-2(1*H*)-quinolinone (Compound **732**);

4-Trifluoromethyl-6-(4-hydroxymethyl)phenyl-2(1*H*)-quinolinone (Compound **734**);

4-Trifluoromethyl-6-(3-acetylphenyl)-2(1*H*)-quinolinone (Compound **735**);

4-Trifluoromethyl-6-(4-ethylphenyl)-2(1*H*)-quinolinone (Compound **736**);

4-Trifluoromethyl-6-(3-ethoxylphenyl)-2(1*H*)-quinolinone (Compound **737**);

4-Trifluoromethyl-6-(3-methylphenyl)-2(1*H*)-quinolinone (Compound **738**);

4-Trifluoromethyl-6-(3-trifluoromethylphenyl)-2(1*H*)-quinolinone (Compound **739**);

4-Trifluoromethyl-6-(3-chlorophenyl)-2(1*H*)-quinolinone (Compound **740**);

4-Trifluoromethyl-6-(3-fluorophenyl)-2(1*H*)-quinolinone (Compound **741**); 4-Trifluoromethyl-6-(2-methylphenyl)-2(1*H*)-quinolinone (Compound **742**);

4-Trifluoromethyl-6-(4-formyl)phenyl-2(1*H*)-quinolinone (Compound **743**);

4-Trifluoromethyl-6-(4-*tert*-butylphenyl)-2(1*H*)-quinolinone (Compound **744**);

4-Trifluoromethyl-6-(2-methoxyphenyl)-2(1*H*)-quinolinone (Compound **745**);

4-Trifluoromethyl-6-(2-fluorophenyl)-2(1*H*)-quinolinone (Compound **746**);

4-Trifluoromethyl-6-(4-acetylphenyl)-2(1*H*)-quinolinone (Compound **747**);

4-Trifluoromethyl-6-(4-methylphenyl)-2(1*H*)-quinolinone (Compound **748**);

4-Trifluoromethyl-6-(4-fluorophenyl)-2(1*H*)-quinolinone (Compound **749**);

4-Trifluoromethyl-6-(4-methoxyphenyl)-2(1*H*)-quinolinone (Compound **750**);

4-Trifluoromethyl-6-(3,5-bis-trifluoromethyl)phenyl-2(1*H*)-quinolinone (Compound **751**);

4-Trifluoromethyl-6-(4-trifluoromethoxyphenyl)-2(1*H*)-quinolinone (Compound **752**);

4-Trifluoromethyl-6-(2,4-dichlorophenyl)-2(1*H*)-quinolinone (Compound **753**);

3-Fluoro-4-trifluoromethyl-6-(2-fluorophenyl)-2(1*H*)-quinolinone (Compound **754**);

3-Fluoro-4-trifluoromethyl-6-(2,4-dichlorophenyl)-2(1*H*)-quinolinone (Compound **755**);

4-Trifluoromethyl-6-(4-hydroxyphenyl)-2(1*H*)-quinolinone (Compound **756**);

4-Trifluoromethyl-6-(4,4,4-trifluoro-1(*E*)-butenyl)-2(1*H*)-quinolinone (Compound **771**);

4-Trifluoromethyl-6-(4,4,4-trifluorobutyro)-2-isopropyloxyquinoline (Compound **772**);

4-Trifluoromethyl-6-(1-hydroxy-4,4,4-trifluorobutyl)-2-isopropyloxyquinoline (Compound **773**);

4-Trifluoromethyl-6-(1-(3,3,3-trifluoropropyl)-1(*E*)-propenyl)-2(1*H*)-quinolinone (Compound **774**);

4-Trifluoromethyl-6-(1-ethyl-1-hydroxy-4,4,4-trifluorobutyl)-2-isopropyloxyquinoline (Compound **775**);

4-Trifluoromethyl-6-(1-ethyl-4,4,4-trifluoro-1(*E*)-butenyl)-2(1*H*)-quinolinone (Compound **776**);

4-Trifluoromethyl-6-(1-ethyl-4,4,4-trifluoro-1(*Z*)-butenyl)-2(1*H*)-quinolinone (Compound **777**);

2-Chloro-4-trifluoromethyl-6-(bis-N,N-2,2,2-trifluoroethyl)aminoquinoline (Compound **778**);

2-Methoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **779**);

2-Isopropyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **780**);

2-Ethoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **781**);

2-Acetyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **782**);

2-(2-Dimethylamino)ethoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **783**);

2-Isobutyryloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **784**);

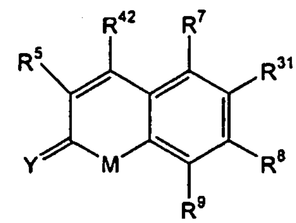
2-(2,2-Dimethyl)propyryloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)-aminoquinoline (Compound **785**);

2-N,N-Dimethylcarbamyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)-aminoquinoline (Compound **786**);

2-Cyano-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **787**);

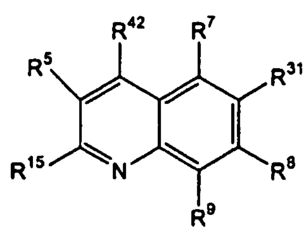
4-Trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone oxime (Compound **788**).

23. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of the formula:



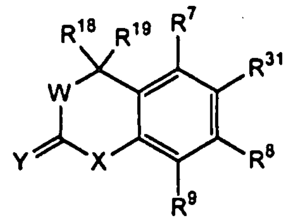
(X)

OR



(XI)

OR



(XII)

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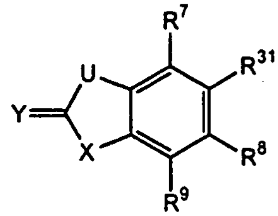


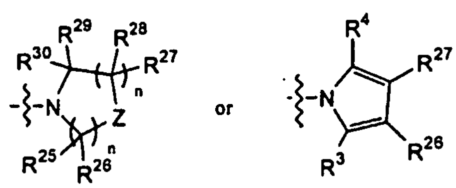
(XIII)

wherein:

R^1 and R^2 are each independently selected from the group of COR^3, CSR^3, SO_2R^3, NO, NR^3R^4, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_2-C_8 haloalkynyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl, C_2-C_8 heteroalkynyl, $(CH_2)_nR^3$, aryl, and heteroaryl, wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, aryl, and heteroaryl are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl; or

R^1 and R^2 taken together form a three- to nine-membered alkyl, alkenyl, heteroalkyl, or heteroalkenyl ring, wherein the alkyl, alkenyl, heteroalkyl, and heteroalkenyl ring are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl; or

R^1 and R^2 are taken together to form one of:



R^3 and R^4 are each independently selected from the group of hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, heteroaryl, and aryl, wherein the alkyl, alkenyl, alkynyl, haloalkyl, heteroalkyl, heteroaryl, and aryl are optionally substituted with halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

R^5 is selected from the group of hydrogen, F, Cl, Br, I, OR^3, SR^3, SOR^3, SO_2R^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 heteroalkyl;

R^7 and R^8 are each independently selected from the group of hydrogen, F, Cl, Br, I, CN, OR^3, NR^3R^4, $NR^3CR^3R^4CONR^3R^4$, $C_n(R^3)_{2n}OR^3$, SR^3, SOR^3, SO_2R^3, NR^3COR^4, C_1-C_8 alkyl, C_1-C_8 haloalkyl, and C_1-C_8 heteroalkyl;

R^9 is selected from the group of hydrogen, F, Br, Cl, I, OR^3, NR^3R^4, SR^3, a C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 heteroalkyl;

R^{11} is selected from the group of hydrogen, F, Br, Cl, I, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, NO_2, CN, CF_3, OR^3, NR^3R^4, SR^3, SOR^3, and SO_2R^3;

R^{15} is selected from the group of hydrogen, F, Br, Cl, I, CN, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, OR^{16}, $NR^{16}R^4$, SR^{16}, CH_2R^{16}, COR^3, CO_2R^3, $CONR^3R^4$, SOR^3, and SO_2R^3;

R^{16} is selected from the group of hydrogen, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_1-C_8 heteroalkyl, aryl, heteroaryl, COR^{17}, CO_2R^{17}, and $CONR^{17}R^{17}$;

R^{17} is selected from the group of hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl and C_1-C_4 heteroalkyl;

R^{18} and R^{19} are each independently selected from the group of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 heteroalkyl; or

R^{18} and R^{19} are taken together to form a three- to seven-membered ring;

R^{22} and R^{23} are each independently selected from the group of hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl and C_1-C_6 heteroalkyl; or

R^{22} and R^{23} are taken together to form a three- to seven-membered ring;

R^{24} is selected from the group of hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, and OR^3;

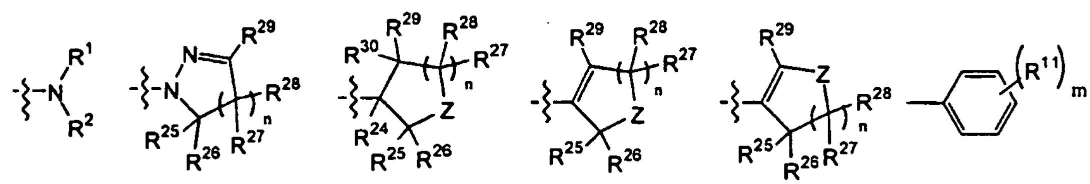
R^{25} through R^{30} are each independently selected from the group of hydrogen, F, Cl, Br, I, OR^3, NR^3R^4, SR^3, SOR^3, SO_2R^3, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, C_2-C_6 alkynyl or C_2-C_6 alkenyl, wherein the alkyl, haloalkyl, heteroalkyl, alkynyl, and alkenyl are optionally substituted with F, Cl, Br, I, OR^3, NR^3R^4, C_1-C_4 alkyl, C_1-C_4 haloalkyl, C_1-C_4 heteroalkyl, aryl or heteroaryl, and wherein the aryl and heteroaryl are optionally substituted with F, Cl, Br, I, CN, NO_2, OH, OCH_3, CF_3 or C_1-C_6 alkyl;

Any two of R^{25}, R^{26}, R^{27}, R^{28}, R^{29} and R^{30} taken together form a three to seven-membered alkyl or alkenyl or heteroalkyl ring; or

Any four of R^{25}, R^{26}, R^{27}, R^{28}, R^{29} and R^{30} taken together form a fused aromatic ring;

R^{31} is selected from the group of hydrogen, F, Cl, Br, I, CN, OR^1, NHR^1, COR^3, CO_2R^3, SR^1, SOR^3, SO_2R^3, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_1-C_8 haloalkyl, C_2-C_8 haloalkenyl, C_1-C_8 heteroalkyl, C_2-C_8 heteroalkenyl, C_2-C_8 alkynyl, C_2-C_8 haloalkynyl, C_2-C_8 heteroalkynyl, $(CH_2)_nR^3$ and heteroaryl, wherein the alkyl, alkenyl, haloalkyl, haloalkenyl, heteroalkyl, heteroalkenyl, allyl, alkynyl, haloallyl, haloalkynyl, heteroalkynyl, $(CH_2)_nR^3$, and heteroaryl are optionally substituted with F, Cl, Br, I, CN, OR^1, NO_2, NR^1R^3, SR^1, SOR^3, SO_2R^3, C_1-C_4 alkyl, C_1-C_4 haloalkyl, or C_1-C_4 heteroalkyl; or

R^{31} represents one of:



R^{42} is selected from the group of hydrogen, F, Cl, Br, I, CH_3, CF_3, CHF_2, CFH_2, CN, CF_2Cl, CF_2OR^3, OR^3, SR^3, SOR^3, SO_2R^3, NR^3R^4, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_4 haloalkyl, C_2-C_4 haloalkenyl, C_2-C_4 haloalkynyl, C_1-C_4 heteroalkyl, C_2-C_4 heteroalkenyl, and C_2-C_4 heteroalkynyl, wherein the alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, aryl, and heteroaryl are optionally substituted with halogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl or C_1-C_4 heteroalkyl;

M is selected from the group of O, S, and NR^{16};

U is selected from the group of O, S, NR^3, $CR^{22}R^{23}$, CR^3R^4O, and CR^3R^4S;

W is selected from the group of O, S, NR^3, and $CR^{22}R^{23}$;

X is selected from the group of O, S or NR^{16}, provided that when R^{31} is aryl or heteroaryl, X is not NR^{16};

Y is selected from the group of O, S, NR^{16}, NOR^{16} and $CR^{16}R^{17}$;

Z is selected from the group of O, S, NR^3, C=O, and $CR^{25}R^4$; or

Z is two hydrogens;

n is 1, 2 or 3; and

m is 1 to 5,

and pharmaceutically acceptable salts thereof.

24. A pharmaceutical composition according to claim 23, wherein the compound is an androgen receptor modulator.

25. A pharmaceutical composition according to claim 24, wherein the compound is an androgen receptor antagonist.

26. A pharmaceutical composition according to claim 24, wherein the compound is an androgen receptor agonist.

27. A pharmaceutical composition according to claim 24, wherein the compound is an androgen receptor partial agonist.

28. A pharmaceutical composition according to claim 23, wherein the compound is a progesterone receptor modulator.

29. A pharmaceutical composition according to claim 28, wherein the compound is a progesterone receptor antagonist.

30. A pharmaceutical composition according to claim 28, wherein the compound is a progesterone receptor agonist.

31. A pharmaceutical composition according to claim 28, wherein the compound is a progesterone receptor partial agonist.

32. A pharmaceutical composition according to claim 23, wherein the composition comprises one or more compounds selected from the group of:

6-Amino-4-trifluoromethyl-2(*1H*)-quinolinone (Compound **200**);

6-Propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **204**);

6-Isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **205**);

6-Isobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **206**);

6-(2,2-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **207**);

6-Cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **208**);

6-(2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **209**);

6-(2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **210**);

6-(2,2-Difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **211**);

6-(2-Chloro-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **212**);

6-Acetylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **213**);

6-Trifluoroacetylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **214**);

6-Benzoylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **215**);

6-Dimethylacetylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **216**);

6-Dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **217**);

6-Diethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **218**);

6-Dipropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **219**);

6-Dibutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **220**);

6-Diisobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **221**);

6-(bis-Cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **222**);

6-(bis-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **223**);

6-(bis-2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **224**);

6-(bis-2-Chloro-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **225**);

6-(bis-2-Bromoethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **226**);

6-(N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **227**);

6-(bis-N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **228**);

6-(N-2,2,2-Chlorodifluoroethyl-N-2,2,2-Trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **229**);

6-(bis-N-2,2-Difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **230**);

6-(N-2,2-Dichloroethyl-N-2,2,2-trichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **231**);

6-(bis-N-2,2-Dichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **232**);

6-(N-2,2-Dichloroethyl-N-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **233**);

6-(N-2,2-Dichloroethyl-N-2,2,2-chlorodifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **234**);

6-(N-Isopropyl-N-methyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **235**);

6-(N-Methyl-N-cyclopentyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **236**);

6-(N-Methyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **237**);

6-(N-Ethyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **238**);

6-(N-Ethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **239**);

6-(N-Ethyl-N-1-methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **240**);

6-(N-Ethyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **241**);

6-(N-Ethyl-N-2,2-dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **242**);

6-(N-Ethyl-N-cyclopentyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **243**);

6-(N-Ethyl-N-1-acetylethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **244**);

(±)-6-(N-Ethyl-N-1-methyl-2-hydroxypropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **245**);

6-(N-Ethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **246**);

6-(N-Ethyl-N-3-furylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **247**);

(±)-6-(N-Ethyl-N-2,2-dimethoxyisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **248**);

6-(N-Isopropyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **249**);

6-(N-2-Hydroxyethyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **250**);

(±)-6-(N-Propyl-N-1-methylbutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **251**);

(±)-6-(N-Propyl-N-1,2-dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **252**);

6-(N-Propyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **253**);

6-(N-Propyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **254**);

(±)-6-(N-Propyl-N-1-methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **255**);

6-(N-2-Hydroxyethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **256**);

6-(N-Isopropyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **257**);

6-(N-Methyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **258**);

6-(N-2,2,2-trifluoroethyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **259**);

6-(N-2,2,2-trifluoroethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **260**);

6-(N-2,2,2-Trifluoroethyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **261**);

(±)-6-(N-2,2,2-Trifluoroethyl-N-1-methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **262**);

(±)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **263**);

(+)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **264**);

(-)-6-(N-2,2,2-Trifluoroethyl-N-2-chloroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **265**);

6-(N-2,2,2-Trifluoroethyl-N-3-furfuryl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **266**);

6-(N-2,2,2-Trifluoroethyl-N-3-thiophenemethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **267**);

6-(N-2,2,2-Trifluoroethyl-N-3,3-dimethylbutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **268**);

6-(N-2,2,2-Trifluoroethyl-N-2-thiophenemethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **269**);

6-(N-2,2,2-Trifluoroethyl-N-2-furfuryl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **270**);

6-(N-Butyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **271**);

6-(bis-N,N-Benzyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **272**);

6-(N-2,2,2-Trifluoroethyl-N-cyclobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **273**);

6-(N-2,2,2-Trifluoroethyl-N-2,2-dichloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **274**);

6-(N-2,2,2-Trifluoroethyl-N-2-chloroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **275**);

6-(N-Benzyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **276**);

6-(N-4-Fluorobenzyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **277**);

6-(N-Propyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **278**);

6-(N-2,2,3,3,3-Pentafluoropropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **279**);

6-Diallylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **280**);

6-(N-Isobutyl-N-allyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **281**);

6-(N-Isopropyl-N-allyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **282**);

6-(N-Allyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **283**);

6-Allylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **284**);

6-(N-Allyl-N-cyclopropylmethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **285**);

6-(N-Allyl-N-2,2,2-trifluoroacetyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **286**);

6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroacetyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **287**);

6-(N-Allyl-N-propyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **288**);

(±)-6-(N-2-Hydroxyisopropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **289**);

(±)-6-(N-Isobutyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **290**);

6-(N-2,2-Difluoroethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **291**);

6-(N-2,2-Dimethylpropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **292**);

6-(N-2,2-Difluoro-2-chloroethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **293**);

6-(N-2,2-Difluoro-2-chloroethyl-N-2,2-difluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **294**);

6-(N-2,2,2-Trifluoroethyl-N-methylsufonyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **295**);

1-Methyl-6-(N-propyl-N-isobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **296**);

1-Methyl-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **297**);

1-Ethyl-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **298**);

6-(N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **299**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **300**);

(±)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **301**);

(+)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **302**);

(-)-6-(N-2,2,2-Trifluoroethyl-N-2,2,2-trifluoroisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **303**);

6-Methoxythiocarbonylmercapto-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **304**);

6-Mercapto-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **305**);

6-(1,1-Dimethyl-2-propynyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **306**);

6-*tert*-Butylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **307**);

6-Bromo-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **308**);

6-Bromo-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **309**);

6- *tert*-Butylamino-2-isopropyloxy-4-trifluoromethylquinolines (Compound **310**);

6-(1-Piperdinyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **311**);

6-(1-Pyrrolidinyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **312**);

6-(1-Morpholino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **313**);

(±)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **314**);

(+)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **315**);

(-)-6-(2-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **316**);

6-(N-phenylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **317**);

6-(N-phenyl-N-ethylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **319**);

6-(N-phenyl-N-ethylamino)-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **320**);

6-(N-phenyl-N-2,2,2-trifluoroethylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **321**);

(±)-6-(3-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **322**);

6-(4-Methyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **323**);

6-(*cis*-3,5-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **324**);

6-(2,6-*cis*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **325**);

6-(2,6-*trans*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **326**);

(±)-6-(2-Methyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **327**);

6-(2,5-*cis*-Dimethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **328**);

(±)-6-(2,5-*trans*-Dimethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **329**);

6-(1-Azepano)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **330**);

(±)-6-(2-Hydroxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)--quinolinone (Compound **331**);

6-(2,5-cis-Dimethyl-1-pyrrolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **332**);

(±)-6-(2-Propyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **333**);

(±)-6-(2-Methoxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **334**);

(±)-6-(2-Ethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **335**);

6-(1-Cycloheptylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **336**);

(±)-6-(2-Ethoxycarbonyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **337**);

(±)-6-(2-Isopropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **338**);

(±)-6-(2-Hydroxycarbonyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **339**);

6-(3,5-*cis*-Dimethyl-1-piperazino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **340**);

(±)-6-(2-Benzyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **341**);

(±)-6-(5-Methyl-2-oxo-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **342**);

(±)-6-(2-(2-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **343**);

(±)-6-(3-Hydroxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **344**);

(±)-6-(3-Acetyloxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **345**);

(±)-6-(3-Hydroxy-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **346**);

6-(1-Indolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **347**);

6-(1-Tetrahydroquinolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **348**);

6-(2-Tetrahydroisoquinolino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **349**);

(±)-6-(1,3,3-Trimethyl-6-azabicyclo[3.2.1]octanyl-6-)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **350**)

(±)-6-(2-Trifluoromethyl-5-*cis*-methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **351**);

(±)-6-(2-Trifluoromethyl-5-*trans*-methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **352**);

6-N-(1-Hydroxyisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **353**);

(±)-6-(2-Trifluoromethyl-5-cis-ethyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **354**);

(±)-6-(2-Trifluoromethyl-5-trans-ethyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **355**);

(±)-6-(5-Methyl-1-oxazolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **356**);

6-(2,5-Dimethyl-1-pyrrolyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **357**);

6-(N-2,2,2-Trifluoroethyl-N-3,3,3-trifluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **358**);

6-(N-3,3,3-Trifluoropropyl)amino-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **360**);

6-bis-N,N-Thiomethoxymethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **361**);

6-bis-N,N-Thiomethoxymethylamino-4-trifluoromethyl-2-thiomethoxymethyloxyquinoline (Compound **362**);

(±)-6-(2,5-*trans*-Diethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **363**);

6-(2,5-*cis*-Diethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **364**);

(±)-6-(2,5-*trans*-Dipropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **365**);

6-(2,5-*cis*-Dipropyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **366**);

6-(2,5-Dipropyl-1-pyrrolo)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **367**);

6-(2,5-*cis*-Dibutyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **368**);

(±)-6-(2,5-*trans*-Dibutyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **369**);

6-(2,6-*cis*- Diethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **370**);

(±)-6-(2,6-*trans*-Diethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **371**);

6-(2,6-*cis*- Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **372**);

(±)-6-(2,6-*trans*-Dimethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **373**);

6-(N-Propyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **374**);

6-Amino-4-methyl-2(1*H*)-quinolinone (Compound **375**);

6-(bis-2,2,2-Trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **377**);

6-(2,5-Dimethyl-1-pyrrolyl)-4-methyl-2(1*H*)-quinolinone (Compound **378**);

(±)-6-(2,5-*trans*-dimethyl-1-pyrrolidino)-4-methyl-2(1*H*)-quinolinone (Compound **379**);

6-(2,5-*cis*-dimethyl-1-pyrrolidino)-4-methyl-2(1*H*)-quinolinone (Compound **380**);

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **381**);

6-(N-2,2,2-Chlorodifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **382**);

6-(bis-N,N-2,2,2-Chlorodifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **383**);

6-(N-2,2,2-Chlorodifluoroethyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **384**);

6-N-Ethylamino-4-methyl-2(1*H*)-quinolinone (Compound **385**);

6-(N-Ethyl-N-2,2,2-trifluoroethyl)amino-4-methyl-2(1*H*)-quinolinone (Compound **386**);

6-N,N-Diethylamino-4-methyl-2(1*H*)-quinolinone (Compound **387**);

6-(bis-2,2,2-trifluoroethyl)amino-4-ethyl-2(1*H*)-quinolinone (Compound **388**);

6-Amino-4-ethyl-2(1*H*)-quinolinone (Compound **389**);

6-(bis-2,2,2-trifluoroethyl)amino-4-isopropyl-2(1*H*)-quinolinone (Compound **391**);

6-Amino-4-isopropyl-2(1*H*)-quinolinone (Compound **392**);

7-Fluoro-6-(bis-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **393**);

7-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **394**);

5-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **395**);

6-Amino-7-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **396**);

8-Fluoro-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **397**);

8-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound 316); 6-Amino-8-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **399**);

8-Fluoro-6-(N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **400**);

8-Fluoro-6-(N-2,2,2-trifluoroethyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **401**);

6-Amino-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **402**);

3-Fluoro-6-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **403**);

3-Fluoro-6-(bis-2,2,2-trifluorofluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **404**);

6-(bis-Isobutylamino)-4-methyl-2(1*H*)-quinolinone (Compound **405**);

3-Fluoro-6-(N-methyl-N-2,2,2-trifluorofluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **406**);

7-Bromo-6-isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **407**);

6-Amino-7-bromo-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **408**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-hydroxy-2(1*H*)-quinolinone (Compound **409**);

6-amino-4-hydroxy-2(1*H*)-quinolinone (Compound **410**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-methoxy-2(1*H*)-quinolinone (Compound **411**);

6-amino-4-methoxy-2(1*H*)-quinolinone (Compound **412**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-4-difluoromethyl-2(1*H*)-quinolinone (Compound **413**);

6-amino-4-difluoromethyl-2(1*H*)-quinolinone (Compound **414**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **415**);

6-amino-2(1*H*)-quinolinone (Compound **416**);

4-Chloro-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **417**);

6-amino-4-chloro-2(1*H*)-quinolinone (Compound **418**);

7-Methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **419**);

5,7-Dimethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **420**);

(*R*)-6-(2-Hydroxymethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **421**);

(*R*)-6-(2-Methoxycarbonyl-1-pyrrolidino)-4-trifluoromethyl-2-isopropyloxyquinoline (Compound **422**);

(*R*)-6-(2-Methoxymethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **423**);

(±)-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **424**);

(±)-6-(2-Cyanothiomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **425**);

(±)-6-(2-Thiomethoxymethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **426**);

(±)-6-(2-Cyanomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **427**);

(±)-6-(2-Bromomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **428**);

(±)-6-(2-Iodomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **429**);

(+)*R*-6-(2-Iodomethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **430**);

(±)-6-(2-Fluoromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **431**);

(+)S-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **432**);

(-)R-6-(2-Chloromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **433**);

(+)*R*-6-(2-Chloromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **434**);

(-)*S*-6-(2-Chloromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **435**);

R-6-(2-Difluoromethyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **436**);

(±)-6-(2*l*-(1*l*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **437**);

(±)-6-(2*l*-(1*u*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **438**);

(±)-6-(2-Formyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **439**);

(±)-6-(2-Difluoromethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **440**);

(±)-6-(2-Aminomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **441**);

(*R*)-6-(2-Vinyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **442**);

(*R*)-6-(2-Formyl-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **443**);

(±)-6-(2-Vinyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **444**);

(±)-6-(2-Benzyloxyethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **445**);

(±)-6-(2-(2,2-Difluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **446**);

(±)-6-(2-Trifluoroacetamidomethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **447**);

(±)-6-(2-(2-Ethoxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **448**);

(±)-6-(2-(4-Trifluoromethyl)benzyloxyethyl-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **449**);

(+)-6-(2*R*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **450**);

(-)6-(2*R*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **451**);

6-(2*S*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **452**);

6-(2*S*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-pyrrolidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **453**);

(±)-6-(2*l*-(1*l*-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **454**);

(±)-6-(2*l*-(1*u*-Hydroxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **455**);

(-)-6-(2*S*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **456**);

(+)-6-(2*R*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **457**);

(+)-6-(2*R*-(1*S*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **458**);

(-)-6-(2*S*-(1*R*-Hydroxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **459**);

(±)-6-(2*l*-(1*l*-Acetyloxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **460**);

(±)-6-(2*l*-(1*u*-Acetyloxyethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **461**);

(±)-6-(2*l*-(1*u*-Methoxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **462**);

(±)-6-(2*l*-(1*l*-Methoxy-2,2,2-trifluoroethyl)-1-piperidino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **463**);

7-Methoxy-6-(N-methyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **464**);

4-Amino-2-methoxy-N-2,2,2-trifluoroethylaniline (Compound **466**);

7-Methoxy-6-(N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **467**);

7-Methoxy-6-(N-ethyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **468**);

7-Hydroxy-6-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **469**);

6-(N-Cyclopropylmethyl-N-2,2,2-trifluoroethyl)amino-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **470**);

6-(N-Cyclopropylmethyl-N-2,2,2-trifluoroethyl)amino-7-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **471**);

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **472**);

6-(N-Isobutyl-N-2,2,2-trifluoroethyl)amino-7-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **473**);

6-(bis-2,2,2-Trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound **474**);

6-Amino-4-trifluoromethylcoumarin (Compound **475**);

(±)-3,4-Dihydro-6-(bis-2,2,2-trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound **476**);

6-(2,2,2-trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound **477**);

6-(N-Isopropyl-N-2,2,2-trifluoroethyl)amino-4-trifluoromethylcoumarin (Compound **478**);

6-N-Isobutylamino-4-trifluoromethylcoumarin (Compound **479**);

6-N,N-Diethylamino-4-trifluoromethylcoumarin (Compound **480**);

6-N,N-Dipropylamino-4-trifluoromethylcoumarin (Compound **481**);

6-N-Propylamino-4-trifluoromethylcoumarin (Compound **482**);

6-(N-Isobutyl-N-propylamino)-4-trifluoromethylcoumarin (Compound **483**);

6-(N-2,2,2-Trifluoroethyl-N-propylamino)-4-trifluoromethylcoumarin (Compound **484**);

1,4-Dihydro-4,4-dimethyl-6-methylamino-1,3-benzo[d]oxazin-2-one (Compound **485**);

6-Amino-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **487**);

1,4-Dihydro-4,4-dimethyl-6-dimethylamino-1,3-benzo[d]oxazin-2-one (Compound **488**);

1,4-Dihydro-4,4-dimethyl-6-dipropylamino-1,3-benzo[d]oxazin-2-one (Compound **489**);

1,4-Dihydro-4,4-dimethyl-6-(bis-N,N-2,2,2-trifluoroethyl)amino-1,3-benzo[d]oxazin-2-one (Compound **490**);

1,4-Dihydro-4,4-dimethyl-6-(N-2,2,2-trifluoroethyl)amino-1,3-benzo[d]oxazin-2-one (Compound **491**);

(±)-1,4-Dihydro-4-methyl-6-diallylamino-1,3-benzo[d]oxazin-2-one (Compound **492**);

(±)-6-Amino-1,4-dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **494**);

6-Amino-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **495**);

6-Diallylamino-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **497**);

3,4-Dihydro-4,4-dimethyl-6-dipropylamino-2(1*H*)-quinolinone (Compound **498**);

3,4-Dihydro-4,4-dimethyl-6-propylamino-2(1*H*)-quinolinone (Compound **499**);

3,4-Dihydro-4,4-dimethyl-6-(N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **500**);

3,4-Dihydro-4,4-dimethyl-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **501**);

3,4-Dihydro-6-(N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **502**);

6-Amino-3,4-dihydro-2(1*H*)-quinolinone (Compound **503**);

3,4-Dihydro-6-(bis-N,N-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone (Compound **505**);

5-(bis-N,N-2,2,2-Trifluoroethyl)amino-3,3-spirocyclohexyl-2-indolone (Compound **506**);

5-Amino-3-spirocyclohexyloxindole (Compound **507**);

7-(bis-N,N-2,2,2-Trifluoroethyl)amino-1,4-benzoxazin-3(4*H*)-one (Compound **508**);

7-amino-1,4-benzoxazin-3(4*H*)-one (Compound **509**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-2,4-dichloroquinoline (Compound **510**);

6-amino-1,4-dichloro-2(1H)-quinolinone (Compound **511**);

7-Amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **512**);

7-Propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **513**);

7-Isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **514**);

7-(2,2-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **515**);

7-(2-Methylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **516**);

7-Methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **517**);

7-Dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **518**);

7-Benzylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **519**);

7-(2,2,3,3,3-Pentafluoropropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **520**);

7-Butylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **521**);

7-Ethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **522**);

7-(N-2,2,2-Trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **523**);

7-Cyclohexylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **524**);

7-Cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **525**);

7-Cyclobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **526**);

7-(2-Hydroxy-2-methylpropionyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **527**);

7-(Trifluoroacetamido)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **528**); 1-Methyl-7-methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **529**);

1-Methyl-7-dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **530**);

1-Methyl-7-(N-methyl-N-isopropylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **531**);

1-Methyl-7-(2,2,2-trifluoromethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **532**);

3-Fluoro-7-(2,2,2-trifluoromethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **533**);

3-Fluoro-7-amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **534**);

3-Fluoro-7-isopropylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **535**);

3-Fluoro-7-cyclopentylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **536**);

3-Fluoro-7-cyclohexylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **537**);

3-Fluoro-7-cyclobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **538**);

3-Fluoro-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **539**);

3-Fluoro-1-methyl-7-(N-methyl-N-isopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **540**);

3-Fluoro-1-methyl-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **541**);

6-Fluoro-7-amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **542**);

6-Fluoro-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **543**);

6-Fluoro-7-isobutylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **544**);

6-Fluoro-1-methyl-7-propylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **545**);

6-Fluoro-1-methyl-7-(N-methyl-N-propylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **546**);

7-Amino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **547**);

7-Isobutylamino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **548**);

7-Propylamino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **549**);

7-(1,1-Dimethyl-3-oxobutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **550**);

7-(1,1,3-Trimethyl-3-hydroxybutyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **551**);

7-(1,1,3-Trimethyl-3-butenylamino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **552**);

7-(1-Phenylaminocarbonylisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **553**);

7-(2-Hydroxy-1,1-dimethylethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **556**);

7-(N-1-Formylisopropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **558**);

7-(1,1-Dimethylallyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **559**);

7-(1,1-Dimethylpropyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **560**);

7-(1-Methyl-1-acetylenylpropyl)amino]-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **561**);

7-(1-Ethyl-1-methylpropyl)amino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **562**);

8-Methyl-7-(3-methyl-2-butenyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **563**);

8-Methyl-7-(3-methylbutyl)amino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **566**);

8-Methyl-7-propylamino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **567**);

8-Methyl-7-isobutylamino-4-(trifluoromethyl)-2(1*H*)-quinolinone (Compound **569**);

7-Amino-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **571**);

7-Isobutylmino-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **574**);

7-(2-Picolylamino)-6-(2,2,2-trifluoroethoxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **575**);

7-Amino-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **576**);

7-Amino-6-ethyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **577**);

7-Amino-6-propyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **580**);

7-Amino-6-*sec*-butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **581**);

7-Amino-6-cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **582**);

6-Ethyl-7-(2,2,2-trifluoroethyl)amino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **585**);

6-Ethyl-7-methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **586**);

6-Ethyl-7-dimethylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **587**);

6-Isobutyl-7-methylamino-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **588**);

7-(1-Morpholino)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **589**);

5-Amino-7-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **592**);

5-Propylamino-7-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **594**);

7-Chloro-5-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **595**);

5-Amino-6-bromo-3,4-dihydro-4-hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **596**);

6-Bromo-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **598**);

6-(bis-N,N-2,2,2-trifluoroethyl)amino-5-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **600**);

6-amino-5-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **601**);

6-(N-2,2,2-Trifluoroethyl)amino-5-propyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **602**);

6-amino-5-propyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **603**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-propyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **604**);

6-(N-2,2,2-Trifluoroethyl)amino-5-ethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **605**);

6-amino-5-ethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **606**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-ethoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **607**);

6-(N-2,2,2-Trifluoroethyl)amino-5-(3,3,3-trifluoropropyloxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **608**);

6-amino-5-(3,3,3-trifluoropropyloxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **609**);

6-(N-2,2,2-Trifluoroethyl)amino-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **610**);

6-amino-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **611**);

6-(bis-N,N-2,2,2-Trifluoroethyl)amino-5-chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **612**);

6-Fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **613**);

6-Chloro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **614**);

6-Isopropyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **615**);

6-Cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **616**);

6-(1- *trans*-Propenyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **617**);

6-Cyclohexyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **618**);

7-Fluoro-6-methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **619**);

5,7-Difluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **620**);

6-Methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **621**);

6-Hydroxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **622**);

6-Benzyloxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **623**);

6-(3-Pentyloxy)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **624**);

6-(1-Hydroxy-3,3,5,5-tetramethyl)cyclohexyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **625**);

6-(3,3,5,5-Tetramethyl)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **626**);

6-(5,5-Dimethycyclopentenyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **627**);

6-(2,2-Dimethycyclopentyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **628**);

6-(1-Hydroxycyclohexyl)-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **629**);

6-Cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **630**);

6-Cyclohexyl-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **631**);

6-Cyclopentenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **632**);
6-Cycloheptenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **633**);
6-Bromo-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **634**);
6-Cyclohexenyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **635**);
6-Cyclohexyl-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **636**);
6-Bromo-7-methoxy-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **637**);
6-Cyclopentyl-3-fluoro-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **638**);
(Z)-6-(1-Propyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **639**);
(E)-6-(1-Propyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **640**);
6-(1-Propyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **641**);
(E)-6-(1-Methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **642**);
(Z)-6-(1-Methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **643**);
(±)-6-(1-Methyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **644**);
(E)-6-(1-Ethyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **645**);
(Z)-6-(1-Ethyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **646**);
6-(1-Ethyl)propyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **647**);
6-(1-Isopropyl-2-methyl-1-)propenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **648**);
6-(1-Isopropyl-2-methyl)propyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **649**);
(Z)-6-(1-Isobutyl-3-methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **650**);
(E)-6-(1-Isobutyl-3-methyl-1-)butenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **651**);
6-(1-Isobutyl-3-methyl)butyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **652**);
6-(1-Propyl)butyl-4-trifluoromethyl-2(1*H*)-thioquinolinone (Compound **653**);
6-(3-Oxo-1-)cyclopentenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **654**);
6-(3-Oxo-1-)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **655**);
6-(3-Oxo-1-)cyclopentenyl-3-methyl-4-difluoromethyl-2(1*H*)-quinolinone (Compound **656**);

6-(3-Oxo-1-)cyclohexenyl-3-mehyl-4-difluoromethyl-2(1*H*)-quinolinone (Compound **657**);

(±)-6-(3-Hydroxy-1-)cyclohexenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **658**);

6-(1-Hydroxy-1,1-diphenyl)methyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **659**);

6-Diphenylmethyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **660**);

6-(3-hydroxy-3-methyl-1-)butynyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **661**);

6-(1-Hydroxy)cyclopentyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **662**);

6-Bromo-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **663**);

6-(1-Cyclopentenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **664**);

6-Cyclopentyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **665**);

6-(1-Hydroxy)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **666**);

6-(1-Cyclohexenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **667**);

6-Cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **668**);

6-(1-Hydroxy)cycloheptyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **669**);

6-(1-Cycloheptenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **670**);

6-(1-Cycloheptyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **671**);

6-(2,6,6-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **672**);

(±)-6-(3,3,5-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **673**);

(±)-6-(3,5,5-Trimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **674**);

(±)-6-(5-Methyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **675**);

(±)-6-(3-Methyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **676**);

(±)-6-(2,6-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **677**);

(±)-6-(2-Bicyclo[2.2.1]heptenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **678**);

(±)-6-(4,5-*trans*-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **679**);

(±)-6-(3,4-*trans*-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **680**);

6-(6,6-Dimethyl-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **681**);

6-(5,5-Dimethyl-1-)cyclopentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **682**);

(±)-6-(3,3,5-*cis*-Trimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **683**);

(±)-6-(3,3,5-*trans*-Trimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **684**);

(±)-6-(3-*cis*-Methyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **685**);

(±)-6-(3-*trans*-Methyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **686**);

(±)-6-(2,6-cis,cis-Dimethyl)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **687**);

(*E*)-6-(1,4-Dimethyl-1-)pentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **688**);

6-(1-Cyclohexenyl)-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **689**);

6-(3-Oxo-1-)cyclopentenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **690**);

6-(3-Oxo-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **691**);

(±)-6-(3-Hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **692**);

(±)-6-(3-*cis*-Hydroxy)cyclohexyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **693**);

(±)-6-(3-Butyl-3-hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-one (Compound **694**);

6-(3-Oxo-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **695**);

6-Bromo-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **696**);

(±)-6-(3-Hydroxy-1-)cyclohexenyl-1,4-dihydro-4,4-dimethyl-1,3-benzo[d]oxazin-2-thione (Compound **697**);

(±)-6-(1-Cyclohexenyl)-1,4-dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **698**);

(±)-6-Bromo-1,4-dihydro-4-methyl-1,3-benzo[d]oxazin-2-one (Compound **700**);

6-(1-Cyclohexenyl)-1,4-dihydro-4,4,5-trimethyl-1,3-benzo[d]oxazin-2-one (Compound **701**);

6-Bromo-1,4-dihydro-4,4,5-trimethyl-1,3-benzo[d]oxazin-2-one (Compound **704**);

6-(1-Cyclohexenyl)-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **705**);

6-Bromo-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **706**);

6-Cyclohexyl-3,4-dihydro-4,4-dimethyl-2(1*H*)-quinolinone (Compound **707**);

(±)-8-Bromo-6-(1-cyclohexenyl)-1,4-dihydro-4-trifluoromethyl-1,3-benzo[d]oxazin-2-one (Compound **708**);

(±)-6,8-Dibromo-1,4-dihydro-4-trifluoromethyl-1,3-benzo[d]oxazin-2-one (Compound **711**);

5-(3-Oxo-1-)cyclohexenyl-3,3-dimethyl-2-indolone (Compound **712**);

5-Bromo-3,3-dimethyl-2-indolone (Compound 542); (±)-5-(3-Hydroxy-1-)cyclohexenyl-3,3-dimethyl-2-indolone (Compound **714**);

(±)-5-(3-Oxocyclohexyl)-3,3-dimethyl-2-indolone (Compound **715**);

(±)-5-(3-Oxocyclohexyl)-3,3-dimethyl-2-indolone (Compound 544); 5-Cyclohexyl-3,3-spirocyclohexyl-2-indolone (Compound **716**);

5-Bromo-3,3-spirocyclohexyl-2-indolone (Compound **717**);

5-Cyclopentyl-3,3-spirocyclohexyl-2-indolone (Compound **718**);

6-(1-Hydroxycyclohexyl)-2(3*H*)-benzothiozolone (Compound **719**);

6-Cyclohexenyl-2(3*H*)-benzothiozolone (Compound **720**);

3,4-Dihydro-6-isopropyl-3-methyl-2(1*H*)-quinazolinone (Compound **721**);

6-Bromo-3,4-dihydro-3-methyl-2(1*H*)-quinazolinone (Compound **722**);

1-Benzyl-6-bromo-3,4-dihydro-3-methyl-2(1*H*)-quinazolinone (Compound **723**);

1-Benzyl-6-cyclohexyl-3,4-dihydro-3-methyl-2(1*H*)-quinazolinone (Compound **724**);

6-(2,3-Difluoro)phenyl-4-trifluoromethyl-2(1*H*)-quinolinone (Compound **725**);

4-Trifluoromethyl-6-(3-nitro)phenyl-2(1*H*)-quinolinone (Compound **727**);

4-Trifluoromethyl-6-(3,5-dichloro)phenyl-2(1*H*)-quinolinone (Compound **728**);

4-Trifluoromethyl-6-(3-fluoro-5-N-hydroxyliminomethyl)phenyl-2(1*H*)-quinolinone (Compound **729**);

4-Trifluoromethyl-6-(3-fluoro-5-formylmethylphenyl)-2(1*H*)-quinolinone (Compound **730**);

4-Trifluoromethyl-6-(3-fluoro-5-cyano)phenyl-2(1*H*)-quinolinone (Compound **731**);

4-Trifluoromethyl-6-(3-fluoro-5-chloro)phenyl-2(1*H*)-quinolinone (Compound **732**);

4-Trifluoromethyl-6-(4-hydroxymethyl)phenyl-2(1*H*)-quinolinone (Compound **734**);

4-Trifluoromethyl-6-(3-acetylphenyl)-2(1*H*)-quinolinone (Compound **735**);

4-Trifluoromethyl-6-(4-ethylphenyl)-2(1*H*)-quinolinone (Compound **736**);

4-Trifluoromethyl-6-(3-ethoxylphenyl)-2(1*H*)-quinolinone (Compound **737**);

4-Trifluoromethyl-6-(3-methylphenyl)-2(1*H*)-quinolinone (Compound **738**);

4-Trifluoromethyl-6-(3-trifluoromethylphenyl)-2(1*H*)-quinolinone (Compound **739**);

4-Trifluoromethyl-6-(3-chlorophenyl)-2(1*H*)-quinolinone (Compound **740**);

4-Trifluoromethyl-6-(3-fluorophenyl)-2(1*H*)-quinolinone (Compound **741**); 4-Trifluoromethyl-6-(2-methylphenyl)-2(1*H*)-quinolinone (Compound **742**);

4-Trifluoromethyl-6-(4-formyl)phenyl-2(1*H*)-quinolinone (Compound **743**);

4-Trifluoromethyl-6-(4-*tert*-butylphenyl)-2(1*H*)-quinolinone (Compound **744**);

4-Trifluoromethyl-6-(2-methoxyphenyl)-2(1*H*)-quinolinone (Compound **745**);

4-Trifluoromethyl-6-(2-fluorophenyl)-2(1*H*)-quinolinone (Compound **746**);

4-Trifluoromethyl-6-(4-acetylphenyl)-2(1*H*)-quinolinone (Compound **747**);

4-Trifluoromethyl-6-(4-methylphenyl)-2(1*H*)-quinolinone (Compound **748**);

4-Trifluoromethyl-6-(4-fluorophenyl)-2(1*H*)-quinolinone (Compound **749**);

4-Trifluoromethyl-6-(4-methoxyphenyl)-2(1*H*)-quinolinone (Compound **750**);

4-Trifluoromethyl-6-(3,5-bis-trifluoromethyl)phenyl-2(1*H*)-quinolinone (Compound **751**);

4-Trifluoromethyl-6-(4-trifluoromethoxyphenyl)-2(1*H*)-quinolinone (Compound **752**);

4-Trifluoromethyl-6-(2,4-dichlorophenyl)-2(1*H*)-quinolinone (Compound **753**);

3-Fluoro-4-trifluoromethyl-6-(2-fluorophenyl)-2(1*H*)-quinolinone (Compound **754**);

3-Fluoro-4-trifluoromethyl-6-(2,4-dichlorophenyl)-2(1*H*)-quinolinone (Compound **755**);

4-Trifluoromethyl-6-(4-hydroxyphenyl)-2(1*H*)-quinolinone (Compound **756**);

6-Bromo-4-methyl-2(1*H*)-quinolinone (Compound **757**);

4-Methyl-6-(3-methoxyphenyl)-2(1*H*)-quinolinone (Compound **758**);

4-Methyl-6-(3-chlorophenyl)-2(1*H*)-quinolinone (Compound **759**);

4-Methyl-6-(3-chloro-2-methylphenyl)-2(1*H*)-quinolinone (Compound **760**);

4-Methyl-6-(2,3-dichlorophenyl)-2(1*H*)-quinolinone (Compound **761**);

4-Methyl-6-(2,4-dichlorophenyl)-2(1*H*)-quinolinone (Compound **762**);

4-Methyl-6-(2-methylphenyl)-2(1*H*)-quinolinone (Compound **763**);

4-Trifluoromethyl-6-phenyl-2(1*H*)-quinolinone (Compound **764**);

4-Trifluoromethyl-6-propio-2(1*H*)-quinolinone (Compound **765**);

4-Trifluoromethyl-6-(1-ethylaminopropyl)-2(1*H*)-quinolinone (Compound **767**);

4-Trifluoromethyl-6-(1-N-ethyl-N-methylaminopropyl)-2(1*H*)-quinolinone (Compound **768**);

4-Trifluoromethyl-6-(1-hydroxy-1-methyl-2-oxopropyl)-2(1*H*)-quinolinone (Compound **769**);

4-Trifluoromethyl-6-(4,4,4-trifluoro-1(*E*)-butenyl)-2(1*H*)-quinolinone (Compound **771**);

4-Trifluoromethyl-6-(4,4,4-trifluorobutyro)-2-isopropyloxyquinoline (Compound **772**);

4-Trifluoromethyl-6-(1-hydroxy-4,4,4-trifluorobutyl)-2-isopropyloxyquinoline (Compound **773**);

4-Trifluoromethyl-6-(1-(3,3,3-trifluoropropyl)-1(*E*)-propenyl)-2(1*H*)-quinolinone (Compound **774**);

4-Trifluoromethyl-6-(1-ethyl-1-hydroxy-4,4,4-trifluorobutyl)-2-isopropyloxyquinoline (Compound **775**);

4-Trifluoromethyl-6-(1-ethyl-4,4,4-trifluoro-1(*E*)-butenyl)-2(1*H*)-quinolinone (Compound **776**);

4-Trifluoromethyl-6-(1-ethyl-4,4,4-trifluoro-1(*Z*)-butenyl)-2(1*H*)-quinolinone (Compound **777**);

2-Chloro-4-trifluoromethyl-6-(bis-N,N-2,2,2-trifluoroethyl)aminoquinoline (Compound **778**);

2-Methoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **779**);

2-Isopropyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **780**);

2-Ethoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **781**);

2-Acetyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **782**);

2-(2-Dimethylamino)ethoxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **783**);

2-Isobutyryloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **784**);

2-(2,2-Dimethyl)propyryloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)-aminoquinoline (Compound **785**);

2-N,N-Dimethylcarbamyloxy-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)-aminoquinoline (Compound **786**);

2-Cyano-4-trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)aminoquinoline (Compound **787**);

4-Trifluoromethyl-6-(bis-2,2,2-trifluoroethyl)amino-2(1*H*)-quinolinone oxime (Compound **788**).

33. A pharmaceutical composition according to claim 23, wherein the composition is formulated for oral, topical, intravenous, suppository or parenteral administration.

34. A method for affecting androgen receptor activity in a mammal, comprising administering to said mammal a compound according to claim 1.

35. A method for affecting progesterone receptor activity in a mammal, comprising administering to said mammal a compound according to claim 1.

36. A method for affecting androgen receptor activity in a mammal, comprising administering to said mammal a compound according to claim 23.

37. A method for affecting progesterone receptor activity in a mammal, comprising administering to said mammal a compound according to claim 23.

38. A method for modulating a process in a mammal mediated by androgen receptors, comprising administering to a mammal a pharmaceutically effective amount of a compound according to claim 1.

39. A method for modulating a process in a mammal mediated by progesterone receptors, comprising administering to a mammal a pharmaceutically effective amount of a compound according to claim 1.

40. A method of modulating a process in a mammal mediated by androgen receptors, comprising administering to a mammal a pharmaceutically effective amount of a composition according to claim 23.

41. A method of modulating a process in a mammal mediated by progesterone receptors, comprising administering to a mammal a pharmaceutically effective amount of a composition according to claim 23.